Identification and expression analysis of small regulatory RNAs in *Yersinia pseudotuberculosis*

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von Barbara Ellen Waldmann

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Zusammenfassung

Die Bedeutung von kleinen regulatorischen RNAs (small RNAs = sRNAs) für die Regulation komplexer bakterieller Netzwerke wurde in den letzten Jahren deutlich. Diese Studie hat sich mit der Identifizierung neuer sRNAs in dem humanpathogenen Bakterium *Yersinia pseudotuberculosis* beschäftigt. Dafür wurde die gesamte RNA von Wildtyp-Bakterien sowie einer Δ*crp* Mutante aus Kulturen isoliert, die sich bei 25°C oder 37°C in der exponentiellen bzw. stationären Wachstumsphase befanden. Mit Hilfe von 454 Pyrosequenzierung und Illumina Sequenzierung konnten 109 neue *trans*-kodierte und 98 neue *cis*-kodierte antisense sRNAs identifiziert werden. Die Mehrzahl dieser sRNAs war in *Y. pseudotuberculosis* und *Y. pestis* konserviert. Die Expression von 47 putativen sRNAs wurde experimentell validiert und deren temperatur- oder wachstumsphasenabhängige Expression bestätigt. Es konnte gezeigt werden, dass die Expression von etwa 50 % dieser sRNAs von dem RNA Chaperon Hfq abhängig ist. Zusätzlich wurde der Datensatz zu bereits publizierten Daten verglichen. Dabei stellte sich heraus, dass die Detektion von sRNAs sowohl von den verwendeten Wachstumsbedingungen, als auch von dem gewählten Stamm, der verwendeten Detektionsmethode und den bioinformatischen Kriterien abhängt.

Interessanterweise zeigte sich im Laufe dieser Arbeit, dass Crp nicht nur als globaler Regulator verschiedene Virulenzgene und eine Vielzahl metabolischer Prozesse von *Y. pseudotuberculosis* kontrolliert, sondern auch die Expression von sRNAs. 91 der neu identifizierten sRNAs wurden direkt oder indirekt von Crp beeinflusst. Die Crp abhängige Expression wurde mittels northern blot Analysen für 13 Kandidaten bestätigt. Crp bindet direkt an die Promotorregion von fünf Kandidaten.

Die durch die Illumina Sequenzierung generierten Daten erlaubten auch eine globale Analyse der Genexpression in Abhängigkeit von der Temperatur, der Wachstumsphase und von dem Crp Protein. Zusätzlich wurden die Ausgangspunkte der Transkription vieler Gene identifiziert.

Die Funktion vieler sRNAs ist abhängig von dem RNA Chaperon Hfq. Diese Studie hat sich auch mit der Regulation der *hfq* Genexpression beschäftigt. Im Gegensatz zu *E. coli* wird die Expression von *hfq* nicht durch die Proteine CsrA und Crp reguliert. Für die Adaptation an oxidativen Stress ist Hfq jedoch relevant. Dieses Stresssignal führte zu reduzierten intrazellulären Hfq Proteinmengen.

Abstract

In the last years it has been realized that bacterial small non-coding RNAs (sRNAs) serve as important components of diverse regulatory circuits. In this study, 109 novel *trans*-encoded sRNAs and 98 novel *cis*-encoded antisense sRNAs were identified in the human pathogen *Y. pseudotuberculosis* YPIII. 454 pyrosequencing and Illumina sequencing of this wild type strain and its isogenic Δ*hfq* and Δ*crp* mutant was carried out after growth at 25°C or 37°C in the exponential or stationary growth phase. The major group of these sRNAs was conserved within *Y. pseudotuberculosis* and *Y. pestis*. The expression of 47 candidate sRNAs was validated experimentally and proved that most of these sRNAs were expressed in a temperature- and/or growth phase-dependent manner. Further, 50 % of the experimentally validated sRNAs showed a dependence on the RNA chaperone Hfq. A comparison to other studies identifying sRNAs in *Yersinia* species showed that some sRNAs overlapped, while some candidates were only detected in the study reported here and vice versa. It could be proven, that this is due to strain specific sRNA expression. Additionally, the growth medium as well as technical and bioinformatic differences influenced the identification.

Interestingly, this study showed that in *Y. pseudotuberculosis* Crp is not only an important regulator controlling virulence and metabolism but is also important for sRNA expression. 91 of the newly identified sRNAs were either directly or indirectly dependent on Crp. The expression pattern of 13 candidates was analyzed by northern blotting. Additionally, a direct interaction of Crp with the upstream region of five of these candidates could be proven.

Illumina sequencing allowed both the identification of novel sRNAs and monitoring the gene expression on a global scale comparing different temperatures, growth phase and the influence of Crp. Additionally, transcriptional start sites were mapped on a global level.

The expression and function of sRNAs is mainly dependent on the RNA chaperone Hfq. Here, the regulation of *hfq* gene expression was investigated. In contrast to *E. coli hfq* expression was not dependent on CsrA or Crp. Furthermore, it could be shown that Hfq is required for resistance to oxidative stress, whereby the stress signal itself was found to influence Hfq protein levels.

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Abbreviation

[w/v]	weight percent
5’ UTR	5’-untranslated region
A	adenosine
approx.	approximately
APS	ammoniumperoxidedisulfate
ATP	adenosine triphosphate
BHI	Brain-Heart-Infusion
Bidest	bidestilled
bp	basepair
C	cytosine
ca.	circa
Ca^{2+}	calcium
cAMP	cyclic adenosinemonophosphate
Cb	carbenicillin
Cm	chloramphenicol
DMEM	Dulbecco’s modified eagle medium
dNTS	desoxyribonucleotides
DNA	deoxyribonucleic acid
et al.	and others, lat. *et alii*
EtOH	ethanol
g	gram
G	guanine
h	hour
Kan	kanamycin
Kb	kilo base
kDA	kilo Dalton
l	liter
LB	Luria Bertani
M	Molar
Max	maximum
MES	2-(N-Morpholino) ethanesulfonic acid

mg	milligram
min	minutes
mio	million
ml	milliliter
mM	millimolar
MOPS	3-(N-Morpholino)-Propanesulfonic acid
mRNA	messenger RNA
nm	nanomolar
nts	nucleotides
OD	optical density
PAGE	polyacrylamide gel electrophoresis
PAP	poly(A)polymerase I
PCR	polymerase chain reaction
RBS	ribosome binding site
RNA	ribonucleic acid
rpm	rotation per minute
RT	room temperature
SD	Shine Dalgarno
SDS	sodium dodecyl sulfate
sec	second
sRNA	small RNA
T	thymine
T3SS	type 3 secretion system
TAP	tobacco acid pyrophosphatase
TCA	tricarboxylic acid
TEX	Terminator Phosphate Dependent Exonuclease
Tris	Tris-(hydroxymethyl)- aminomethane
µg	microgram
µl	microliter
µM	micromolar
vs.	versus

1 Introduction

During their life cycle, bacteria need to rapidly react to changing environmental signals such as temperature, pH, osmolarity, different ion composition, and oxidative stress. Especially enteropathogenic bacteria, such as the human pathogen *Yersinia pseudotuberculosis (Y. pseudotuberculosis)*, most often face two distinct environmental conditions: 1. They have to be able to survive outside the host, facing changing growth conditions such as temperature shifts and low nutrient content, 2. They have to survive insight the host facing the innate and adaptive immune system. These bacteria have established complex regulatory networks to orchestrate these cellular changes as well as to control expression of virulence genes required for the colonization and persistence within the host.

In order to survive and use the available resources most efficiently, bacteria need to be able to sense environmental signals, to transduce them within the cell, to integrate and to amplify signals. Adaptation to a special environmental condition can imply the on- or offset of specific metabolic or stress resistance pathways. A wide range of mechanisms has evolved to perform these functions. Regulation can occur at many different steps e.g. activation or repression of transcription, post-transcriptionally by modulating the stability of transcripts or the translation efficiency or by regulation of the assembly, stability, and processing of the mature protein. Further, the protein activity may be altered by e.g. phosphorylation or methylation of the protein.

Transcriptional regulation can be achieved by several mechanisms. Alternative sigma factors specifically bind to promoter regions upon environmental signals. Further, DNA-binding proteins bind to specific sites on the DNA and can either prevent the binding of RNA-polymerase or can help to recruit RNA-polymerase to this specific site. The DNA structure itself also plays an important role and the state of supercoiling alters the DNA availability for DNA binding proteins.

Post-transcriptional regulation represents control steps following transcription. The changed transcript stability and translation efficiency can be regulated by intrinsic mechanisms. In many cases, secondary structure rearrangements take place affecting the ribosome binding site (RBS), which in turn alters the translational efficiency. In addition, small regulatory RNAs (sRNA) can bind to the mRNAs and alter both transcription stability and translation efficiency. A benefit of this regulation type is a much faster adaption to changing environmental signals.

Preformed mRNA can rapidly be translated leading to higher protein levels, or translation is rapidly shut of and the protein is no longer produced. In many cases both transcriptional and post-transcriptional regulation are combined.

In the last decade it became more and more clear that not only transcriptional regulation but also gene regulation by sRNAs plays a major role in many bacteria. Novel techniques such as high-throughput sequencing opened the possibility to identify a wide range of sRNAs, which has been carried out for several bacterial species.

1.1 Post-transcriptional regulation by small regulatory RNAs

Small regulatory RNAs are present in all domains of life. These RNA species are normally 50-3500 nucleotides (nts) in length and are mainly divided in two classes. The *trans*-encoded sRNAs are encoded between two transcriptional units and in many cases their target is encoded at a distinct site in the chromosome. Nearly all identified and well-characterized sRNAs belong to this class e.g. MicF, Spot42, GlmY, and GlmZ (Ikemura and Dahlberg, 1973; Mizuno *et al.*, 1984; Kalamorz *et al.*, 2007; Reichenbach *et al.*, 2008). Furthermore, sRNAs might be encoded in *cis* meaning that the sRNA is encoded at the same site as a transcriptional unit. To further characterize these sRNAs, *cis*-encoded sRNAs are split up into three subgroups. mRNA leader structures are 5' regions, which are transcribed together with the mRNA but are not translated. These transcripts may fold into secondary structures and function as riboswitches or RNA thermometers. Similar, UTRs can exist at the 3' end of an mRNA. *Cis*-encoded antisense sRNAs are encoded in the opposite direction of a transcriptional unit and show complete complementarity to the target mRNA. The last subgroup encompasses *cis*-encoded sense sRNAs. These sRNAs are transcribed in sense direction within a transcriptional unit and thereby share the same sequence. They are not able to bind to the mRNA of the ORF but they may function similar to *trans*-encoded sRNAs. So far their real impact on bacterial gene regulation is not understood (Schluter *et al.*, 2010) (Figure 1). This chapter focuses on *trans* and *cis*-encoded antisense sRNAs and their way of action.

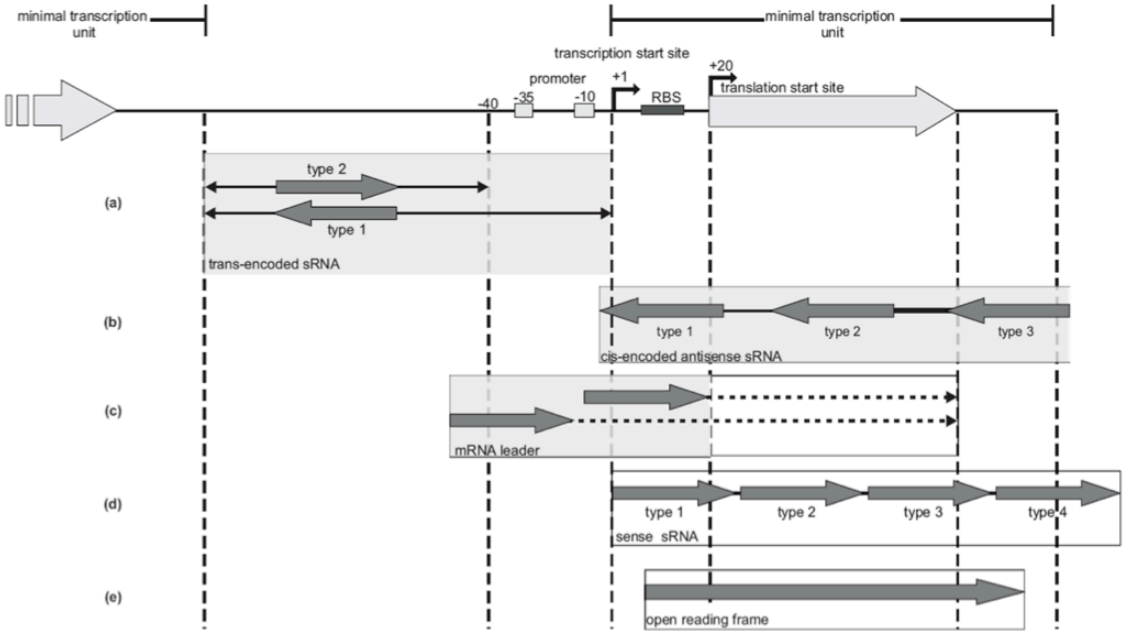


Figure 1: Classification of bacterial sRNAs (Schluter *et al.*, 2010)**.** (a) *trans*-encoded sRNAs are encoded between two transcriptional units and at a different site in the chromosome as their target mRNA. (b) *cis*-encoded antisense sRNAs are transcribed in the opposite direction as a transcriptional unit. (c) mRNA leader structures are 5' untranslated regions in front of an ORF while (d) sense-encoded sRNAs are transcribed from within a transcriptional unit.

1.1.1 *Cis*-encoded antisense RNAs

Antisense-encoded sRNAs (asRNA) are encoded at the same site in the genome as their target and therefore show perfect complementarity. To classify asRNAs is only possible by their location since the mechanisms of these sRNAs are very diverse. asRNAs might either be located in the 3' or 5' UTR of their target mRNA or they are encoded internally. If two different genes encoded in the same direction carry long and overlapping 3' or 5' UTRs and an asRNA is encoded in this region, the expression of both neighboring genes might be connected via the asRNA. In contrast to *trans*-encoded sRNAs asRNAs can vary in size from 100-3500 nts (Georg and Hess, 2011).

Up to now three major mechanisms applied by asRNA have been described: 1. They influence the stability of their target mRNA, 2. They modulate the rate of translation, and 3. They terminate transcription.

Changing the stability of the mRNA transcript can either lead to reduced or increased stability. The asRNA GadY in *Escherichia coli (E. coli)* is encoded in the 3' UTR of the *gadX* mRNA. *gadX* is encoded in a bicistronical operon together with *gadW* and mediates the acid stress response system (*gad* system) (Opdyke *et al.*, 2004). Upon binding of GadY the bicistronical transcript is cleaved into two more stable transcripts by RNase III (Figure 2 A) (Takada *et al.*, 2007; Tramonti *et al.*, 2008; Opdyke *et al.*, 2011).

The IsrR sRNA in *Synechrocystis* 6803 regulates the stability of the *isiA* mRNA which leads to a massive reorganization of the photosynthesis apparatus under iron stress. The expression of *isiA* is induced upon iron, redox, and light stress and the resulting mRNA is very stable (Dühring *et al.*, 2006; Legewie *et al.*, 2008). Binding of IsrR to the *isiA* mRNA leads to the degradation of both sRNA and mRNA. Induced transcription of *isiA* titrates IsrR out and liberated *isiA* mRNA can be translated. Thereby, a delay in IsiA production upon stress but a fast depletion of IsiA upon stress recovery is ensured (Dühring *et al.*, 2006).

Modulating the translation rate also effects the stability of the target mRNA (Georg and Hess, 2011). This mechanism is applied by SymR controlling *symE* translation. *symE* belongs to the SOS system in *E. coli* coding for a toxin like RNA endonuclease. SymR binds to the 5' UTR of the *symE* transcript overlapping the RBS and the AUG, what prevents *symE* translation and the degradation of the transcript is induced (Kawano *et al.*, 2007) (Figure 2 B). *In vitro* experiments suggested, that the asRNA aspocR in *Listeria monocytogenes* inhibits the translation of *pocR* on transcriptional level (Mellin *et al.*, 2013).

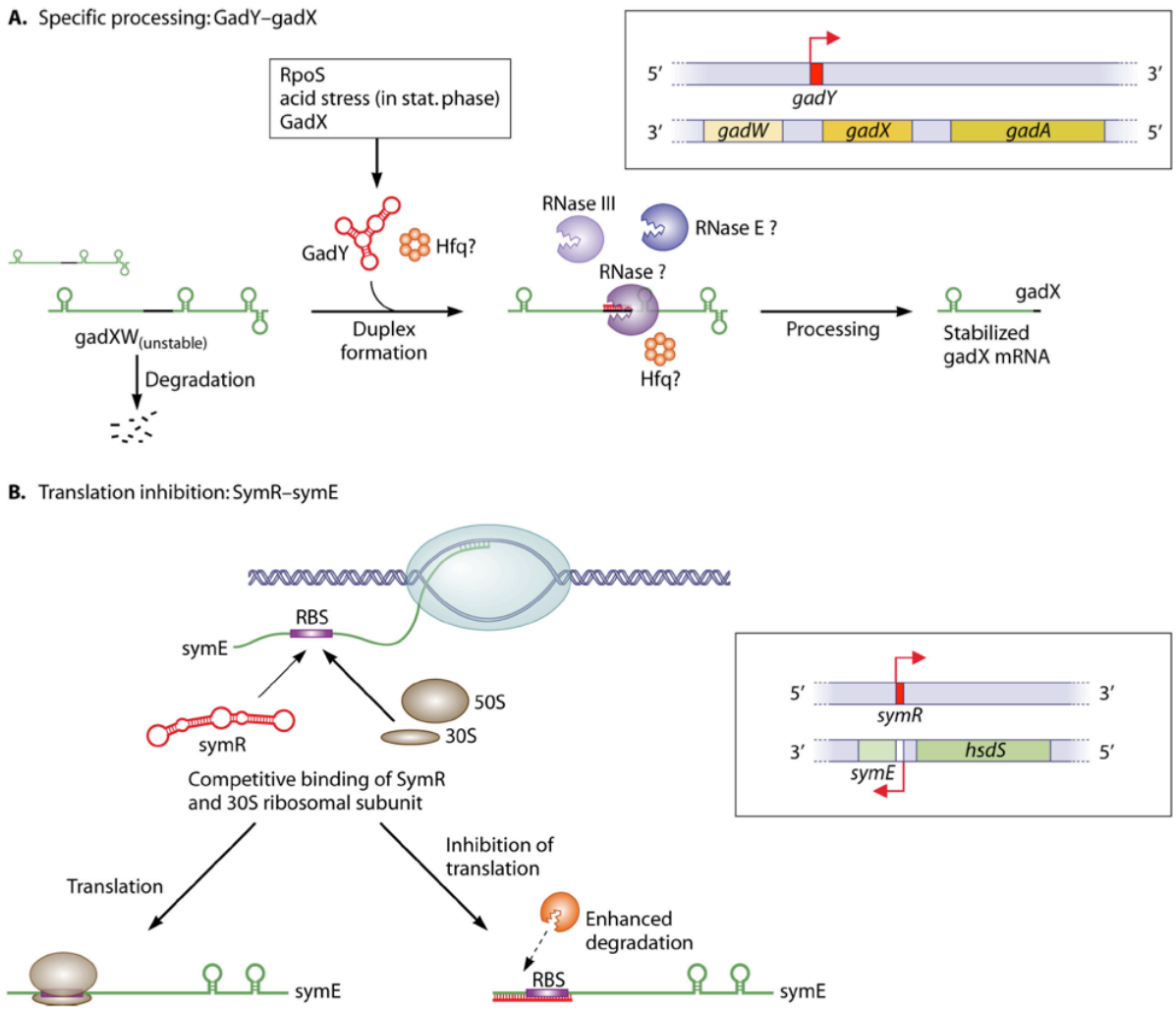


Figure 2: Mechanisms employed by asRNAs (modified from Georg and Hess, 2011). (A) The *gadXW* transcript gets specifically cleaved upon binding of GadY resulting in two more stable transcripts. (B) Translation of the *symE* mRNA is inhibited by binding of SymR. SymR binds to a region spanning the RBS and the AUG of the *symE* transcript.

So far the last identified mechanism employed by asRNA is transcriptional termination. This can be accomplished by direct interaction of the asRNA with its target mRNA. In *Helicobacter pylori* the 5' *ureB*-sRNA is encoded in the opposite direction as *ureB*. *ureB* is cotranscribed with *ureA* upon low pH. If a neutral pH is present the antisense sRNA is transcribed and binds to the 5'-end of the *ureB* mRNA resulting in transcription termination, to ensure that urease function is only present in low pH conditions (Figure 3) (Wen *et al.*, 2013).

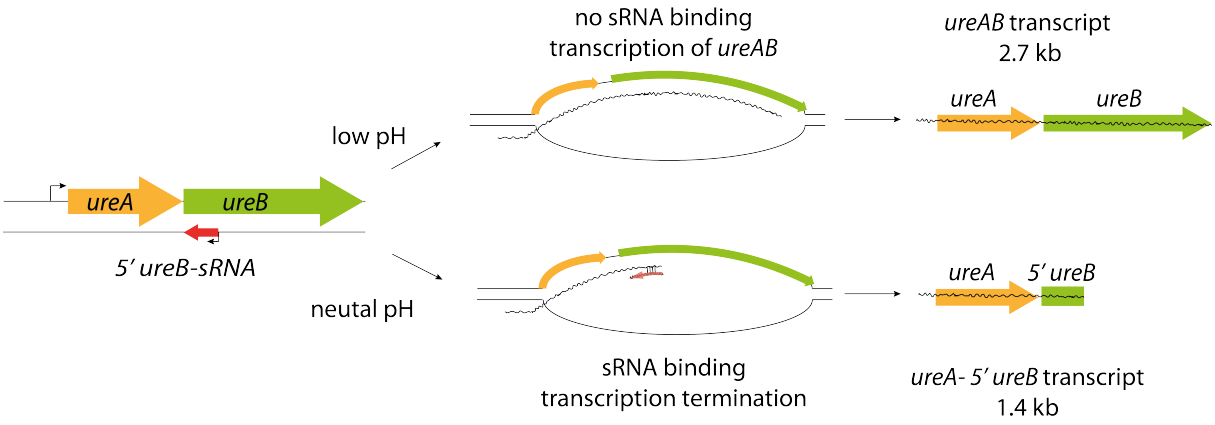


Figure 3: Transcriptional termination achieved by asRNAs. Binding of the *5' ureB*-sRNA to the *ureAB* transcript leads to transcription termination at neutral pH (Wen *et al.*, 2013).

1.1.2 *Trans*- encoded sRNAs

In contrast, *trans*-encoded sRNAs are localized at a different position in the genome as their target. Many of these sRNAs function via base pairing but others function via protein interaction. In case of direct mRNA binding these sRNAs only show a partial complementarity and in most cases form duplexes over short stretches with mismatching positions. Due to their partial complementarity *trans*-encoded sRNAs can have several targets and thereby form their own regulon (Storz *et al.*, 2011). They vary in size from 50-500 nts and in most cases require the RNA chaperone Hfq to function properly (see section 1.1.3). The main modules are conserved between nearly all *trans*-encoded sRNAs (Figure 4). The 3' end is structured and most often followed by a poly(U) motive, which promotes Rho-independent transcription termination. Towards the 5' end they carry an Hfq binding site as well as a seed region which is responsible for target recognition and duplex formation (Storz *et al.*, 2011).

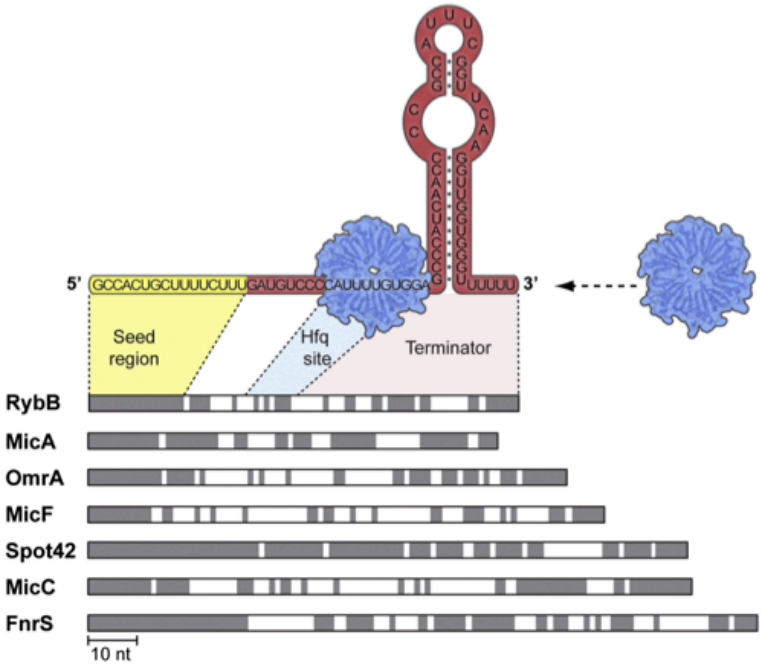


Figure 4: General modules of *trans*-encoded sRNAs (modified from Storz et al., 2011). They consist of a seed region, an Hfq binding site and a terminator region. Some well-characterized examples are aligned to the general modules. The most widely conserved regions of the sRNAs are illustrated in grey.

Trans-encoded sRNAs are often classified by their mode of action.

The first class of *trans*-encoded sRNAs change the availability of the RBS by directly binding in its vicinity (Figure 5). The sRNA RNAIII of *Staphylococcus aureus* interacts with the *hla* mRNA and has a positive effect on its translation. *hla* encodes for an α-toxin and the mRNA forms a hairpin masking the SD sequence. Binding of RNAIII upstream of the SD sequence leads to structural rearrangements liberating the RBS (Morfeldt *et al.*, 1995). In *E. coli* binding of OxyS to the *fhlA* transcript has a negative impact. The interaction between OxyS and *fhlA* is facilitated by 7-9 nts localized in two hairpin regions of the sRNA. They bind to the mRNA covering the SD and 25 nts downstream of the RBS resulting in translation inhibition (Argaman and Altuvia, 2000).

The PcrZ sRNA in *Rhodobacter sphaeroides* binds to the *bchN* mRNA. *bchN* is involved in the photosynthesis of this bacterium and overproduction of PcrZ leads to reduced protein production. The PcrZ binding site spans nts -3 - +29 of the *bchN* mRNA and masks the RBS for ribosome binding (Mank *et al.*, 2012).

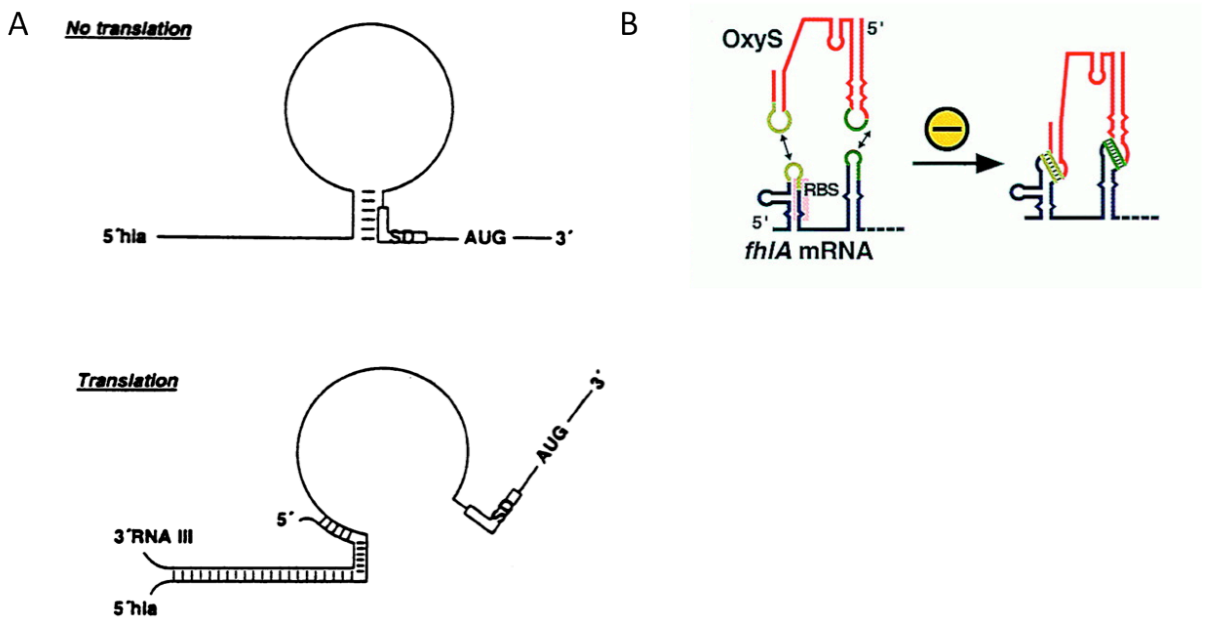


Figure 5: Mechanisms used by RNA III and OxyS (Morfeldt *et al.*, 1995; Altuvia and Wagner, 2000)**.** (A) Binding of RNAIII to the *hla* mRNA leads to a rearrangement liberating the SD, while (B) OxyS binding to the *fhlA* mRNA blocks the SD.

The second mechanism employed by *trans*-encoded sRNAs is the binding further up- or downstream of a translation initiation site, which alters the translation rates. The sRNA SR1 of *Bacillus subtilis* uses this mechanism to control the translation rate of the *ahrC* mRNA, which belongs to the arginine catabolic network. In its activated state the *ahrC* mRNA forms a complex structure where the RBS is free for ribosome binding. Binding of SR1 far downstream of the RBS leads to remarkable structural changes and translation can no longer be initiated (Heidrich *et al.*, 2007). The *tisB* mRNA carries a ribosome standby site (RSS), which is important for translation initiation. The primary transcript is cleaved 46 nts from its 3' end resulting in an active form where ribosomes bind to the RSS. Most probably, ribosome sliding along the mRNA leads to the recognition of the RBS and translation is initiated. Binding of the sRNA IstR-1 to the active version of *tisB* blocks the RSS for ribosome binding and translation is repressed (Darfeuille *et al.*, 2007) (Figure 6).

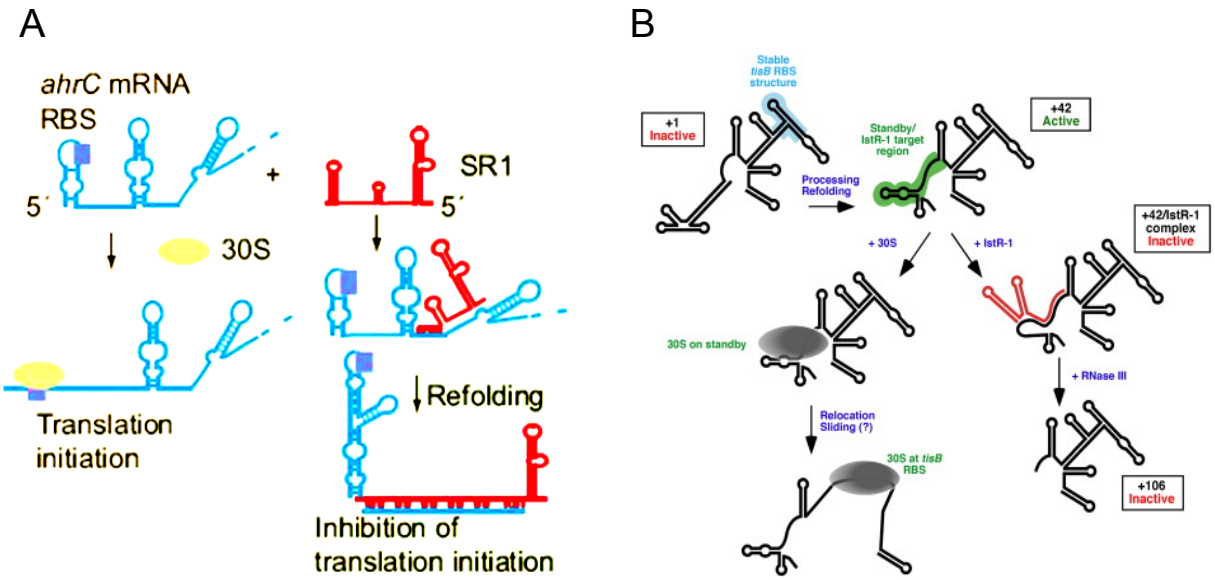


Figure 6: SR1 and IstR-1 binding to their target mRNAs (modified from Darfeuille *et al.*, 2007; Brantl, 2009). (A) Binding of SR1 leads to a refolding of the *ahrC* mRNA and inhibition of translation inhibition. (B) Binding of IstR-1 blocks the RSS of the *tisB* mRNA which in turn inhibits translation.

The third class of *trans*-encoded sRNAs facilitates their function by protein binding (Figure 7). The CsrA protein together with the small regulatory RNAs CsrB and CsrC belongs to the carbon storage regulatory system, which is also called Rsm system. CsrA is an RNA binding protein that binds to (N)GGA sequence motives located in the untranslated leader and/or translated region of target transcripts. One of the binding sites overlaps the ribosome binding site leading to blockage of ribosome binding upon CsrA binding. In most cases, blockage of translation results in degradation of the target mRNA (Liu and Romeo, 1997; Weilbacher *et al.*, 2003; Babitzke and Romeo, 2007). The sRNAs CsrB and CsrC contain 9-18 GGA motives and are able to sequester multiple CsrA dimers from its target mRNAs. The ribosome binding site becomes free and translation can occur.

Similarly, the 6S RNA of *E. coli* binds the RNA polymerase. The sRNA is highly expressed in the stationary growth phase and was found to be associated with the RNA polymerase holoenzyme carrying the sigma factor σ^{70} (Wassarman and Storz, 2000). The secondary structure of this sRNA simulates the DNA open complex. It is hypothesized that the 6S RNA sequesters the RNAP from the DNA and thereby acts as a global transcriptional regulator. Since the sRNA is highly expressed in stationary growth it is generally believed that the 6S

RNA switches expression from exponential to stationary growth (Wassarman and Saecker, 2006; Gildehaus *et al.*, 2007).

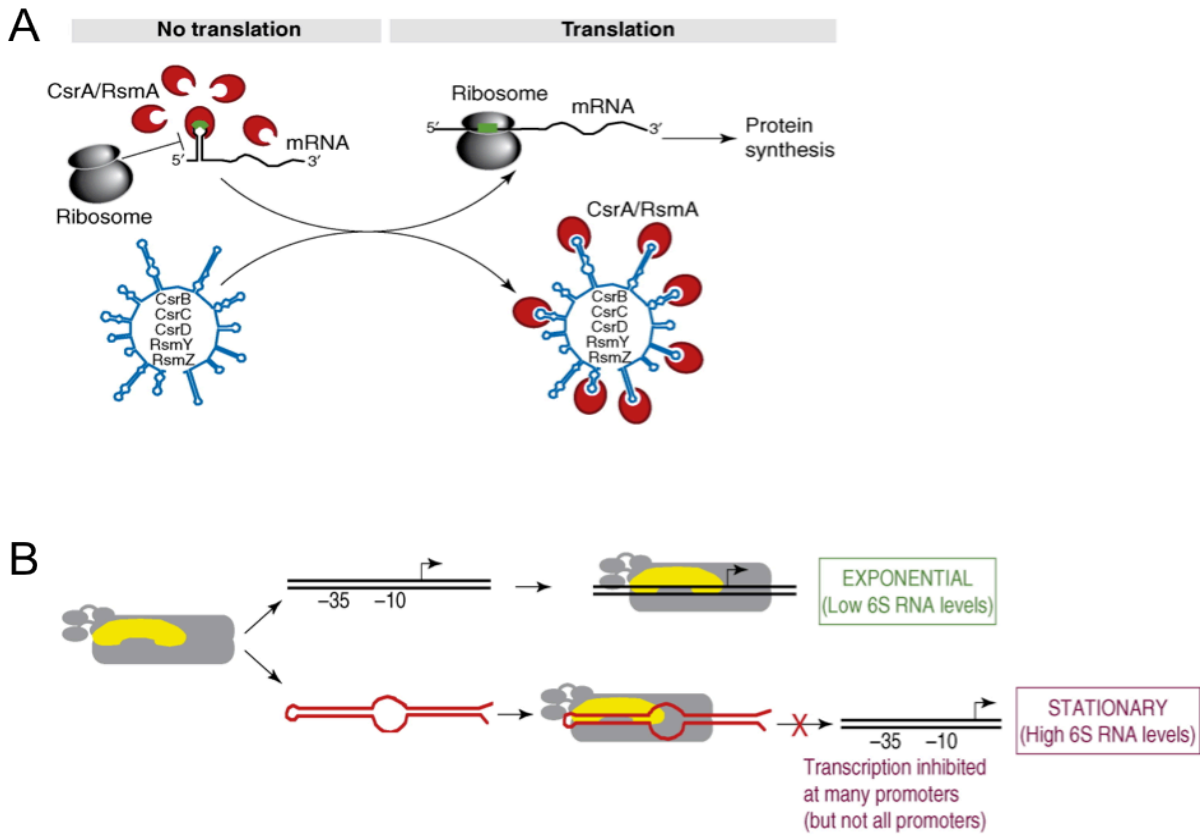


Figure 7: Protein binding sRNAs (modified from Toledo-Arana et al., 2007; Wassarman, 2007). (A) The sRNAs CsrB and CsrC bind the CsrA protein thereby sequestering it from its target mRNA, which often activates translation. (B) The 6S RNA mimics the DNA open complex. The RNAP binds to the RNA and transcription is inhibited.

Trans-encoded sRNAs may also act by changing the stability of their target mRNA. In *E. coli* the sRNA RyhB is involved in iron homeostasis (Figure 8). One of its targets is *sodB*. In the proposed model the binding of RyhB together with Hfq to the RBS leads to inhibition of ribosome binding and thereby prevents translation. Subsequently, the degradosome is recruited and processing can take place far downstream from the site where the mRNA-sRNA duplex was formed. This model also allows translating ribosomes to be cleared of the mRNA before processing takes place. Thereby, accumulation of cleaved transcripts harboring stalled ribosomes is prevented (Prévost *et al.*, 2011).

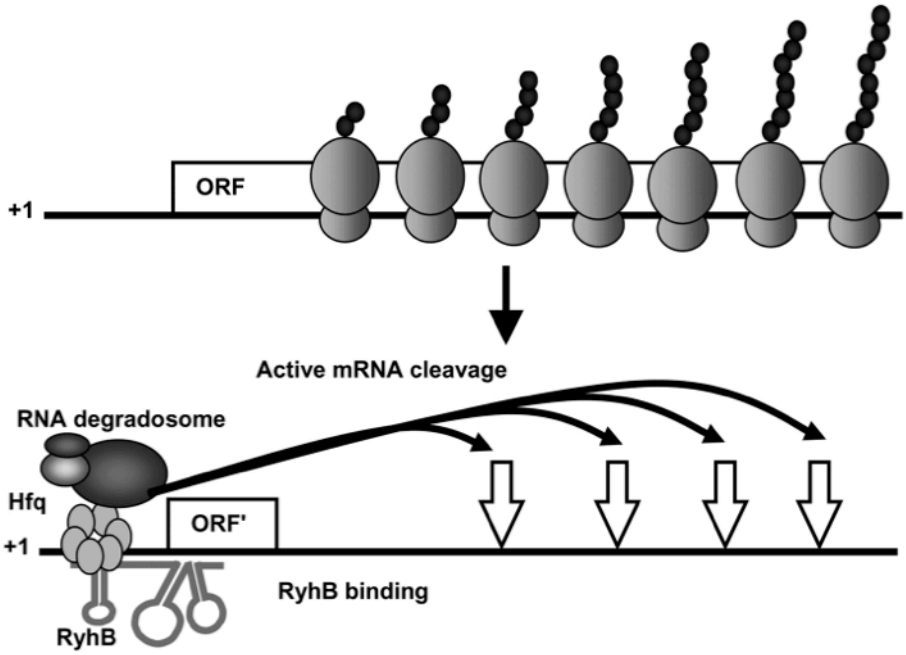


Figure 8: Mechanism applied by RyhB (modified from Prévost et al., 2011). Binding of RyhB and Hfq leads to an inhibition of translation. Ribosomes are cleared of the mRNA and degradation is achieved by the degradosome.

A recent study identified an sRNA in *Salmonella*, which induces Rho-dependent transcription termination. *chiPQ* is encoded in a bicistronical operon and binding of the *trans*-encoded sRNA ChiX to the 5' UTR of *chiP* inhibits translation, thereby uncoupling transcription and translation. This uncoupling makes the mRNA susceptible for Rho-dependent transcription termination (Bossi *et al.*, 2012).

Another mechanism applied by *trans*-encoded sRNAs is the removal of stalled ribosomes from an mRNA. SsrA functions both as tRNA and mRNA and helps to release stalled ribosomes from an mRNA that carries no stop codon. SsrA first functions as a tRNA and its bound alanine is transferred to the nascent protein. Subsequently, SsrA is translocated in the ribosome, releases the mRNA and functions as mRNA. It encodes for ten amino acids, which tag the nascent protein for further degradation (Keiler *et al.*, 1996). For its function the SmpB protein is necessary, which binds to SsrA (Karzai *et al.*, 1999) (Figure 9).

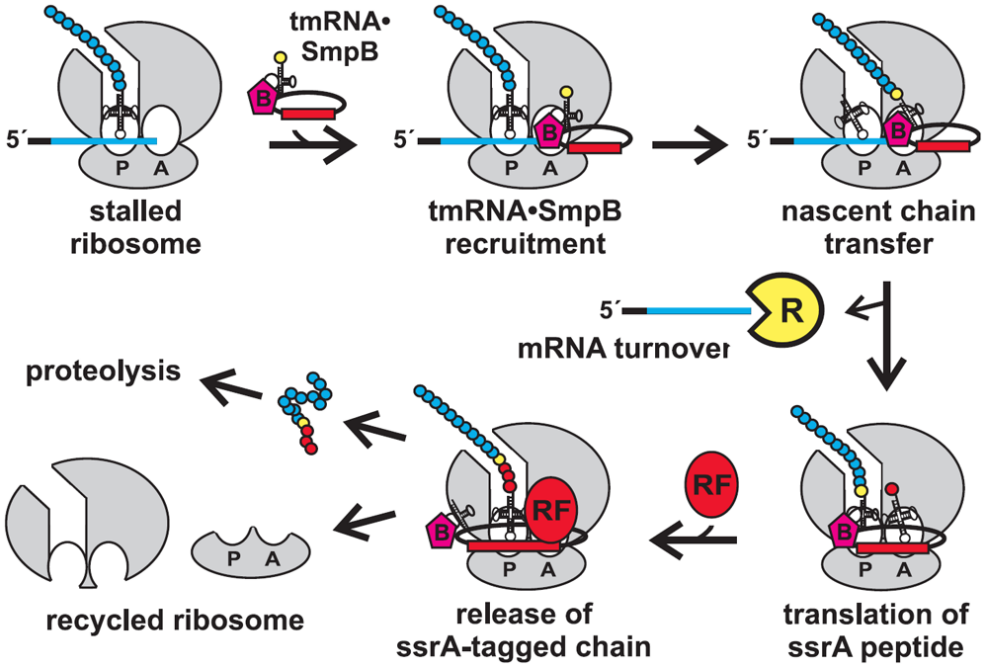


Figure 9: Mode of action of the SsrA sRNA. SsrA binds to stalled ribosomes as tRNA (modified from Janssen and Hayes, 2012). Subsequently, it functions as mRNA and the nascent protein is tagged by a degradation signal. Both the nascent protein and the mRNA are degraded (R = RNase, RF = release factor).

1.1.3 The RNA chaperon Hfq

In many cases the function of *trans*-encoded sRNAs was shown to be strongly dependent on the RNA chaperone Hfq. Research on Hfq started in the late 1960s where it was found to be a host factor involved in the regulation of Qβ phage replication. It was shown that Hfq binds 3' ends of RNAs and it is required for the initiation of – stand RNA synthesis of the Qβ phage (Franze de Fernandez *et al.*, 1968; Franze de Fernandez *et al.*, 1972). In the '90s and the following years Hfq was more intensively studied regarding its influence on bacterial pathogenicity and the identification of the protein structure.

1.1.3.1 Structure and function of Hfq

The Hfq protein belongs to the superfamily of Lsm proteins. These proteins are present in all three domains of life and their conserved structure is one of their major characteristics (Achsel *et al.*, 2001). They form a ring–like structure, which in case of Hfq is formed by a homohexamer (Figure 10 C) (Sauter *et al.*, 2003). The monomer of the protein consists of

five β strands (β_{1-5}), which are separated by five loops forming a strong bended antiparallel β–sheet. On top of the open barrel an α-helix is located (Figure 10 B). On primary sequence level Lsm proteins consist of two conserved sequence motives forming the conserved β-strand elements. The motive Sm1 encompasses the first three β–sheets, while Sm2 encompasses β–sheet 4-5 (Figure 10 A) (Hermann *et al.*, 1995). Hfq contains three RNA binding sites, two located at opposite sites (proximal and distal binding site) and one located at the lateral site of the protein. The distal binding site is responsible for the binding of the target mRNA and it specifically recognizes purine-rich sequences. In *E. coli* the distal site preferentially recognizes an ARN sequence in mRNAs (A: binding of adenosine to adenosine specificity site; R: binding of any purine to the purine selectivity site; N: binding of any nucleotide to the non discriminatory entry/exit site) (Link *et al.*, 2009).

The proximal site is responsible for sRNA binding and recognizes uridine rich sequences. In most cases these uridine rich parts are located in the 3' end of the sRNA so that Hfq recognizes predominantly 3'-ends of sRNAs (Schumacher *et al.*, 2002).

The third RNA binding site at the lateral site of the protein consists of several conserved polar residue which interact with internal uridine rich sequences in single-stranded RNA (Sauer *et al.*, 2012). Given that Hfq is formed by six monomers six lateral binding sites are present.

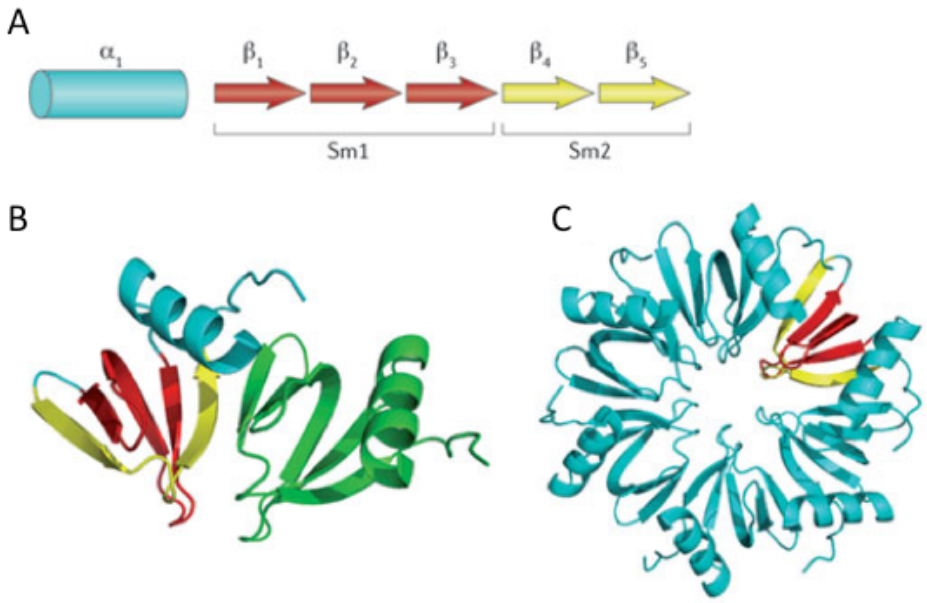


Figure 10: The structure of the Hfq protein (modified from Vogel and Luisi, 2011). (A) Secondary structure elements of the Hfq protein. (B) Protein structure of the Hfq monomer. $\beta_{1\text{-}3}$ are shown in red forming the inner part of the β-sheet. $\beta_{4\text{-}5}$ are shown in yellow and lie in the periphery of the β-sheet forming hydrogen bonds with β-strands of the neighboring monomer (shown in green). The α-helix is shown in blue. (C) Homohexamere of the Hfq protein.

The RNA binding model is illustrated in Figure 11. The 3' ends of sRNAs interact with the proximal site of Hfq and thereby anchor the sRNA to the protein. Furthermore, intrinsic uridine-rich motifs interact with the lateral binding site, which furthermore stabilizes the binding of the sRNA to Hfq. Complex formation of the sRNA with an mRNA results in the release of the sRNA from the lateral binding site but the sRNA remains anchored to Hfq by the proximal binding site. Whether the sRNA or the mRNA binds first to the Hfq protein is not experimentally verified (Sauer, 2013).

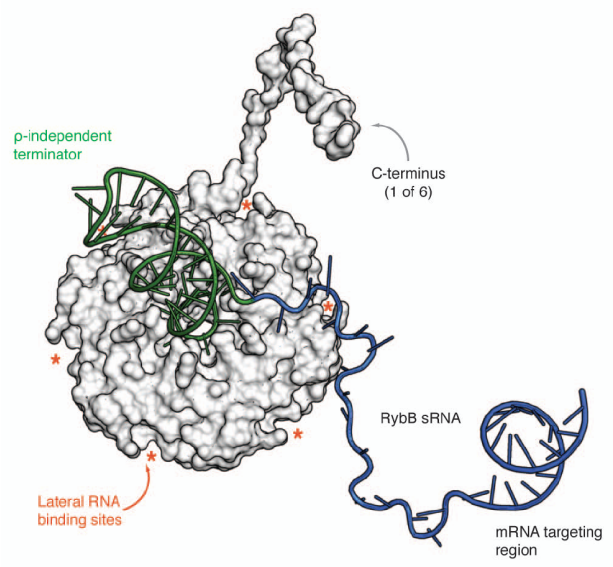


Figure 11: Model of Hfq/sRNA binding at the proximal site (Sauer, 2013). The Hfq protein is depicted as surface representation and the C-terminal part of only one Hfq protein is indicated. The sRNA RybB was modeled into the proximal site and binds with its ρ-independent terminator loop into the proximal site (green), while parts of the single stranded region (blue) bind partially to the lateral site of the protein (indicated by *). Binding of and interaction with the mRNA is not shown.

Functionally, Hfq can mediate regulation by several general mechanisms (Figure 12). The binding of Hfq together with an sRNA can have both positive and negative effects on translation initiation. In some cases Hfq facilitates sRNA binding close to the RBS of its target and therefore ribosome binding is prevented leading to translation inhibition (e.g. binding of OxyS to the *fhlA* mRNA (Argaman and Altuvia, 2000)). In other cases Hfq-sRNA binding leads to structural rearrangements that free the RBS and therefore initiate translation (e.g. binding of DsrA to the *rpoS* mRNA (Majdalani *et al.*, 1998)). Furthermore, binding of Hfq to an sRNA in many cases leads to the stabilization of the sRNA and protects it from RNase E degradation while in other cases the binding of Hfq to sRNAs or mRNAs leads to the recruitment of an RNase and RNA degradation (Vogel and Luisi, 2011). The last described mechanism of Hfq action is the recruitment of the poly(A)polymerase I (PAP). This enzyme polyadenylates RNA and the resulting poly(A) terminus is a signal for RNA degradation (Hajnsdorf and Régnier, 2000; Mohanty *et al.*, 2004).

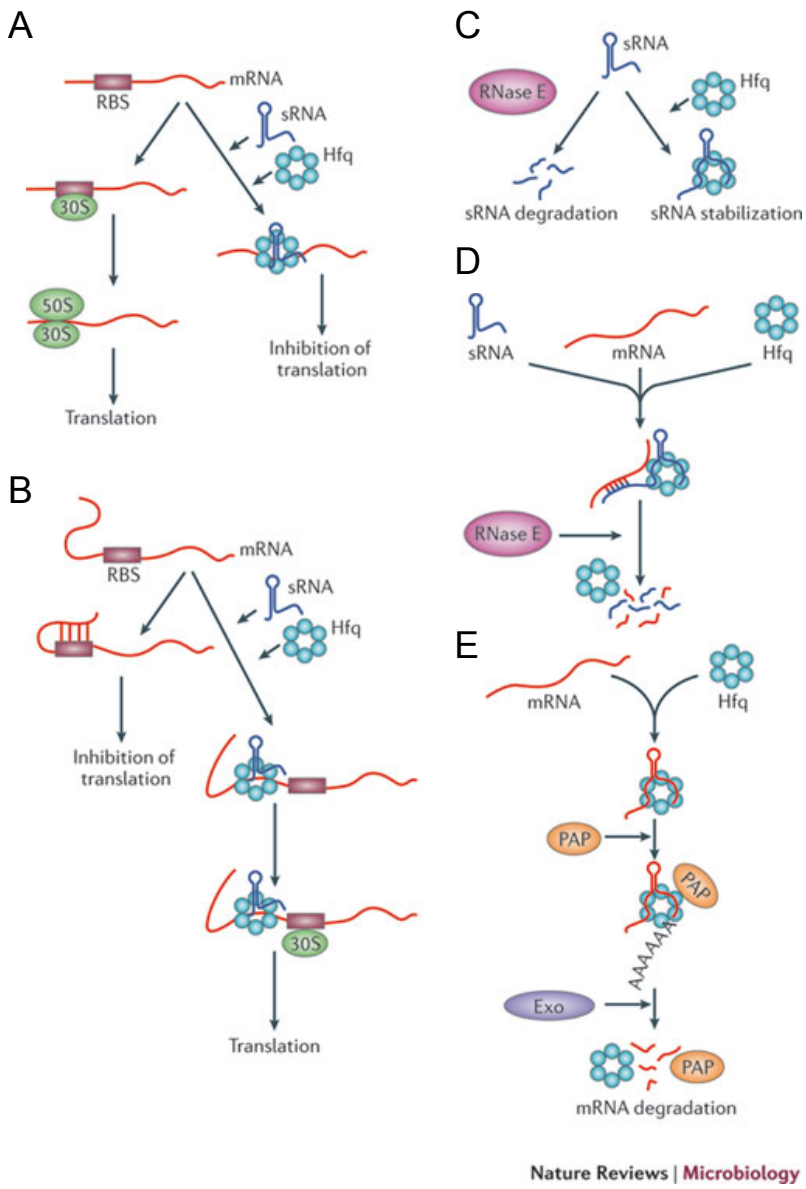


Figure 12: Mode of action of Hfq (Vogel and Luisi, 2011). Binding of Hfq together with an sRNA can lead to (A) translation inhibition or (B) structural rearrangements that free the RBS and initiate translation. Furthermore, Hfq-binding can lead to (C) stabilization of sRNAs or (D) favors the degradation of both sRNA and mRNA. (E) Binding of Hfq to an mRNA can also lead to recruitment of PAP which polyadenylates the mRNA marking it for degradation.

1.1.3.2 Regulation of Hfq Expression

In *E. coli* the *hfq* gene is part of the *amiB-mutC-miaA-hfq-hflX-hflK-hflC* operon (Franze de Fernandez *et al.*, 1968; Franze de Fernandez *et al.*, 1972), which shows 79% homology to the *Y. pseudotuberculosis amiB-mutC-miaA-hfq-hflX-hflK-hflC* operon. The expression control of

the *E. coli hfq* gene is illustrated in figure 13. Transcription is driven from three independent promoters. Promoter P3 is located closest to the start codon and drives transcription 68 nucleotides (nts) upstream of the start codon. Together with P2, which induces expression at position -419, P3 is controlled in a σ^{70}-dependent manner. The transcription controlled by P1 starts -1001 nts upstream of the P3 transcriptional start site and it was shown that this promoter is controlled by the heat shock sigma factor σ^{32} (Tsui *et al.*, 1996). In addition, *hfq* transcription is controlled by the negative transcription regulator Crp. Together with cAMP (cyclic adenosine monophosphate), Crp is able to bind close to promoter P3 at position -104 to -89 and inhibits transcription (Lin *et al.*, 2011). In *Shigella flexneri* it was demonstrated that DksA influences *hfq* expression in a positive manner. DksA is known to regulate transcription during stringent growth in response to increasing ppGpp conditions. Together with ppGpp DksA binds a region around P2 and induces transcription most likely by direct binding to the RNA polymerase and stabilizing the open complex (Paul *et al.*, 2004; Sharma and Payne, 2006).

Expression of *hfq* is not only regulated on the transcriptional level but also post-transcriptionally. The RNA-binding protein CsrA binds a region 49 to 61 nucleotides downstream of the transcriptional start site (P3) overlapping the SD sequence. Thereby, ribosomes are prevented from binding to the mRNA leading to degradation most likely by RNase E (Vecerek *et al.*, 2005; Baker *et al.*, 2007). The SD sequence of the *hfq* mRNA is flanked by two hairpin structures that are build at position +20 to +35 (h1) and +95 to +114 (h2). Hairpin h2 is involved in the post-transcriptional regulation of *hfq* expression by the Hfq protein itself. Hfq binds two regions in its own mRNA (site A: +13 to +18; site B: +72 to +48) and the formation of h2 is necessary for this binding. Site B directly overlaps with the SD sequence and similar to CsrA Hfq binding prevents ribosome-binding. Interestingly, binding to site A is already sufficient to inhibit translation even though it does not cover the RBS (Vecerek *et al.*, 2005).

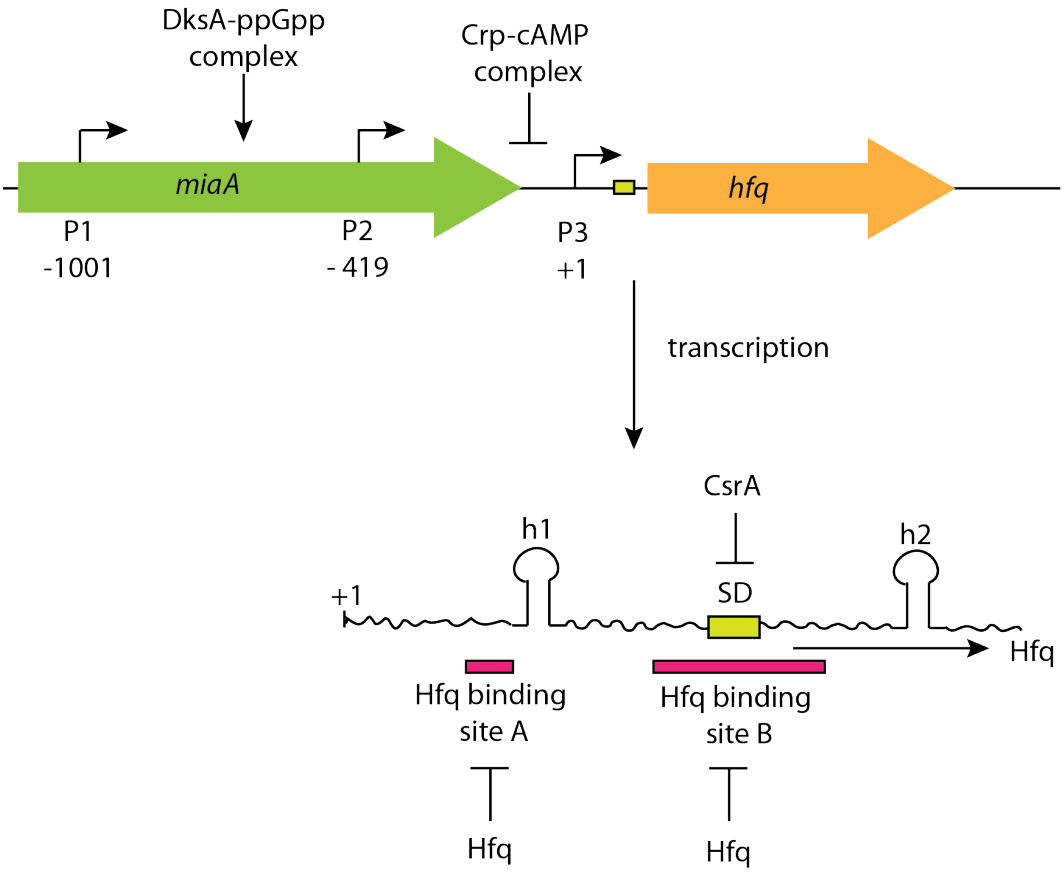


Figure 13: Expression control of the *hfq* gene. Transcription is controlled by the σ^{70}-dependent promoter P3 and P2 and by the heat shock promoter P1. Furthermore, the DksA-ppGpp complex positively influences transcription, while the Crp-cAMP complex has a negative effect. Post-transcriptional regulation is achieved by CsrA binding to the RBS which inhibits translation and by negative Hfq autoregulation (Tsui *et al.*, 1996; Paul *et al.*, 2004; Vecerek *et al.*, 2005; Sharma and Payne, 2006; Baker *et al.*, 2007; Lin *et al.*, 2011).

1.2 The genus *Yersinia* – a pathogen to study bacterial gene regulation

The human pathogen *Y. pseudotuberculosis* is a rod-shaped, Gram negative, facultative anaerobic bacterium that can grow in a temperature range from 4°C to 43°C. Its optimal growth temperature is 25°C. It belongs to the genus *Yersinia,* which encompasses 17 species of which *Y. pseudotuberculosis, Y. pestis* and *Y. enterocolitica* are human pathogens (Carniel, 2003). *Y. pestis* was first isolated by Alexandre Yersin (1863-1943).

Y. enterocolitica is the oldest species of the pathogenic *Yersinia*. *Y. pseudotuberculosis* evolved from this species ca. 41 - 186 mio years ago (Achtman *et al.*, 1999; Skurnik *et al.*, 2000; Achtman *et al.*, 2004). Both pathogens are gastrointestinal pathogens, which are taken

up orally by contaminated water or food. They can cause gut- and lymph-associated diseases (Yersiniosis) such as diarrhea, enterocolitis, and mesenterial lymphadenitis (Bottone, 1997). In rare cases systemic infections and autoimmune diseases such as reactive arthritis and erythema nodosum can occur. Both species carry the virulence plasmid pYV.

After uptake of contaminated water or food, *Y. pseudotuberculosis* is able to survive the acidic condition in the stomach and pass the intestinal tract until it reaches the terminal part of the small intestine, the ileum, where the microfold cells (M-cells) are located (Bottone, 1997; Naktin and Beavis, 1999; Dube, 2009). These cells are not covered with microvilli at their apical site and they are specialized to transport macromolecules and pathogenic material by endo- and phagocytosis from the lumen of the intestine to the underlying lymphatic tissue, the Peyer's patches. The bacteria are normally flagellated and carry smooth lipopolysaccharides as well as the non-fimbrial protein invasin on their surface. Invasin is one of the most important adhesion and invasin molecules of *Y. pseudotuberculosis* and helps the bacteria to bind to and invade into the M-cells.

After transmigration through the M-cells, *Y. pseudotuberculosis* colonizes the Peyer's patches, where the bacteria face the innate immune system represented by dendritic cells, macrophages and lymphocytes, which take up pathogenic material (Hanski *et al.*, 1989; Grutzkau *et al.*, 1990; Neutra *et al.*, 1999; Jang *et al.*, 2004). In this ongoing infection phase, the bacteria switch the expression of their virulence genes and express the *Yersinia* adhesin A (YadA) as well as a type III secretion system (T3SS) and effector proteins (*Yersinia* effector proteins = Yop) (Viboud and Bliska, 2005; Trosky *et al.*, 2008). From the Peyer's patches the bacteria spread into deeper tissues such as liver, spleen, and kidney (Marra and Isberg, 1996a; Barnes *et al.*, 2006) (Figure 14). The initial infection phase encompasses the passage of the bacteria into the ileum and *in vitro* expression of the corresponding virulence factors is simulated by growth at 25°C in the stationary growth phase. Expression of virulence factors produced during ongoing infection is simulated by growth at 37°C in exponential growth phase.

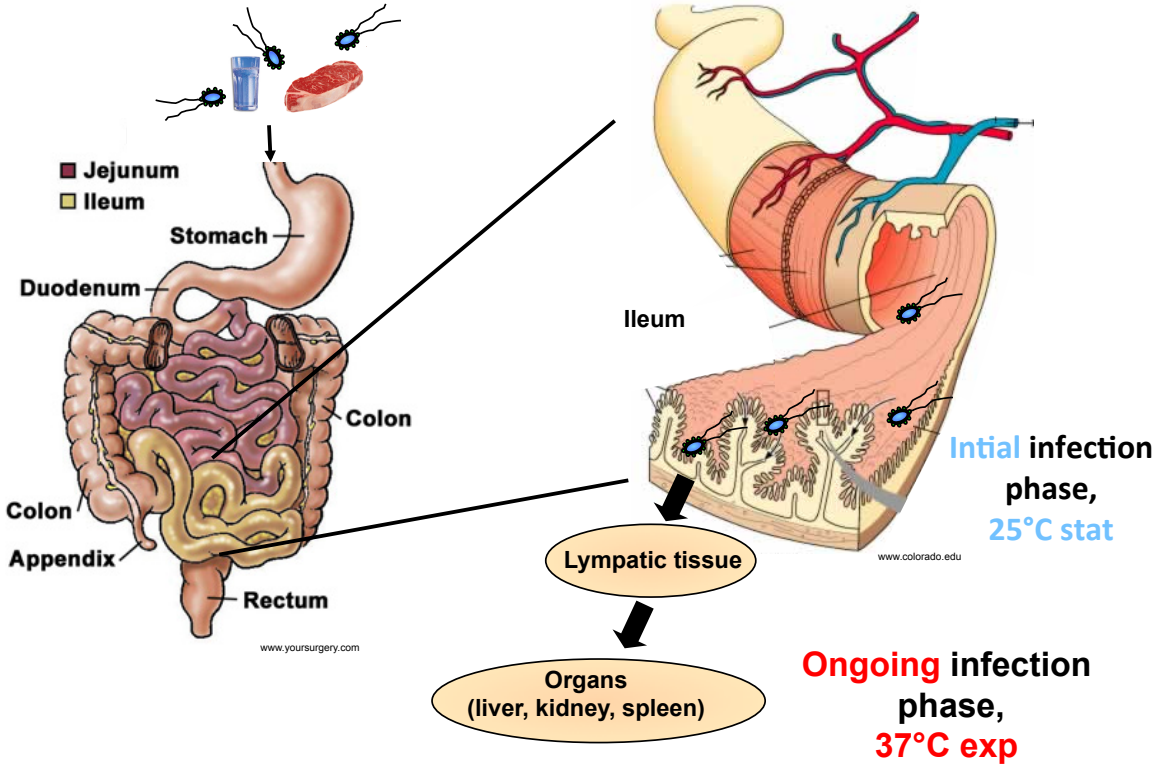


Figure 14: Infection route of *Y. pseudotuberculosis* (modified from www.yoursurgary.com and www.colorado.edu). The bacteria are taken up orally by contaminated water or food. After the passage of the stomach they reach the terminal part of the small intestine (ileum), where they penetrate the epithelial layer and colonize the underlying lymphatic tissue (early infection phase). Subsequently, the bacteria are able to spread in the host and colonize deeper tissues such as liver, spleen, and kidney (late infection phase).

Y. pestis and *Y. pesudotuberculosis* share 97% homology of their chromosome. Therefore, *Y. pseudotuberculosis* is considered "the mother of the bubonic plague", since *Y. pestis* evolved from *Y. pseudotuberculosis* 1,500-20,000 years ago (Achtman *et al.*, 1999; Wren, 2003; Chain *et al.*, 2004). Even though the genome sequence of both species is highly homologous the bacteria cause completely distinct diseases. *Y. pestis* is highly virulent in humans and rodents. It is transferred by the bite of an infected flea and is transmitted into the blood stream. The bacteria migrate to the lymphatic tissue, where they proliferate extracellular and subsequently lead to septicemia, bubonic or pneumonic plague (Prentice and Rahalison, 2007). In addition to the pYV virulence plasmid, *Y. pestis* carries two

additional plasmids pFLA and pPLA which help the bacteria to survive in the flea and the blood stream of the human host (Cornelis, 1994; Chain *et al.*, 2004).

Beside the strong differences in their infection route and disease pattern, all pathogenic *Yersinia* species share common features. All three pathogens show a tropism for lymphatic tissues (Naktin and Beavis, 1999) and are able to efficiently counteract and evade the host immune system by the inhibition of phagocytosis by macrophages and neutrophils. Furthermore, they are able to prevent cell lysis by the complement system (Straley *et al.*, 1993; Heesemann, 1994).

During their life cycle all pathogenic *Yersinia* face distinct environmental influences such as different temperature, pH, other microbes, and the host immune system. All three pathogens have to respond appropriately to these changing environmental conditions in order to survive. The following chapters focus on the function of virulence genes of *Y. pseudotuberculosis* and the regulation of their expression.

1.2.1 Important virulence factors of *Y. pseudotuberculosis*

1.2.1.1 Adhesins and invasins of *Yersinia*

The chromosomally encoded primary invasion factor invasin belongs to the intimin family of adhesins (Figure 15). The C-terminal domain of the protein interacts with β_1 integrins and leads to a downstream signaling resulting in a cytoskeleton rearrangement in the eukaryotic cell (Leong *et al.*, 1991; Clark *et al.*, 1998; Hamburger *et al.*, 1999; Dersch and Isberg, 2000). This rearrangement triggers the uptake of the bacteria by a zipper like mechanism (Isberg and Van Nhieu, 1995; Dersch and Isberg, 2000).

In *Y. enterocolitica in vivo* analysis showed, that invasin is only necessary in the early stage of infection. Deletion of this protein resulted in reduced colonization of the Peyer's patches but not of deeper organs (Pepe and Miller, 1993; Marra and Isberg, 1996b). However, recent data indicated that invasin in *Y. pseudotuberculosis* is necessary throughout the whole infection process (Geyer, unpublished).

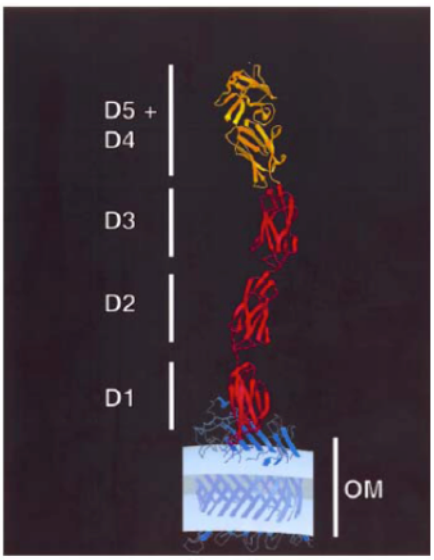


Figure 15: Crystal structure of *Y. pseudotuberculosis* invasin (Isberg *et al.*, 2000)**.** Invasin consists of five C-terminal β-stranded domains (D1-D5) and is anchored in the bacterial membrane by its N-terminus. The domains D4 and D5 are responsible for interaction with the host membrane and are crucial for bacterial uptake.

In addition to the primary invasion factor invasin several other invasin-like proteins have been identified. The function of all of these factors is not understood but it is known that InvB/Ifp as well as InvC are important for host colonization (Pisano *et al.*, 2012). Furthermore, *Y. pseudotuberculosis* carries the chromosomally encoded protein Ail, which is necessary for adhesion and serum resistance (Kolodziejek *et al.*, 2007; Bartra *et al.*, 2008). The pH6 antigen (PsaA) is responsible for hemagglutination and adhesion to mammalian cells (Yang and Isberg, 1997).

After *Yersinia* has colonized the Peyer's patches the bacteria are able to spread into deeper tissues of the human body. During this stage of the infection adhesion to and invasion into human cells is mediated by YadA, which is encoded on the virulence plasmid pYV (Figure 16). YadA aggregates are located at the surface of the bacterial membrane and are able to interact with the extracellular matrix proteins fibronectin, collagen, and laminin via a bridging mechanism (Eitel and Dersch, 2002; Heise and Dersch, 2006). YadA is necessary for persistence of *Y. pseudotuberculosis* in the lung and dissemination into deeper tissues. Further, it helps to bind to and target neutrophils for Yop translocation (Paczosa *et al.*, 2013).

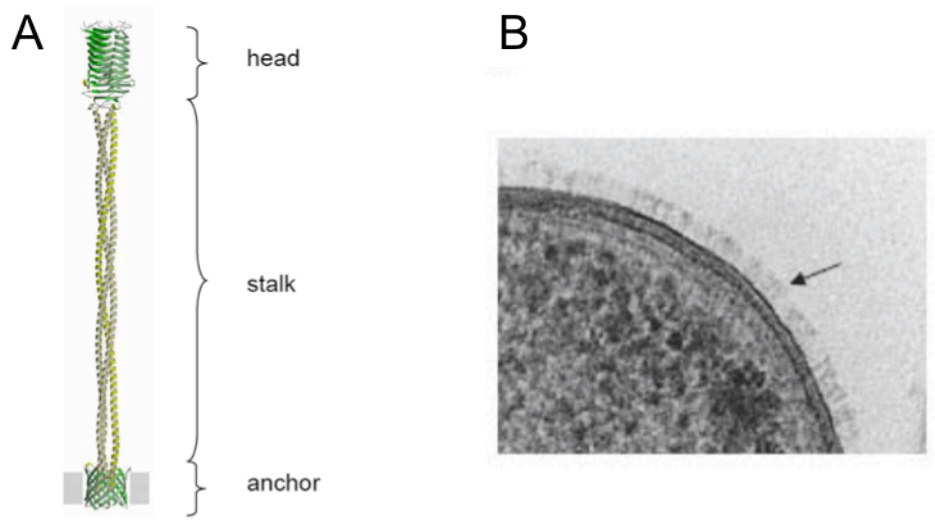


Figure 16: YadA of *Y. enterocolitica* (Hoiczyk *et al.*, 2000; Koretke *et al.*, 2006)**.** (A) Crystal structure of YadA. The protein contains of a head, stalk and anchor domain. (B) Electron microscopic picture of *Y. enterocolitica* expressing YadA. The molecule is distributed all over the cell.

1.2.1.2 The type III secretion system and the Yop effector proteins

After the penetration of the epithelial layer, *Y. pseudotuberculosis* needs to defend itself against the innate immune system. Macrophages and neutrophils are located in the Peyer's patches to take up infectious material (Neutra *et al.*, 1999; Jang *et al.*, 2004). Therefore, *Y. pseudotuberculosis* possesses effector proteins that target multiple signal pathways of the host cell, leading to altered gene expression of inflammatory signals. These factors are injected by the type III secretion system composing of a needle-like structure build by the pYV-encoded Ysc proteins (Cornelis, 1998). The tip of the needle is formed by the proteins YopB, YopD, and LcrV, which contact host cells and form a pore in its membrane (Cheng and Schneewind, 2000). The Yop effector proteins are either translocated through or along this needle structure or they are responsible for the efficient translocation of other effector proteins (Viboud and Bliska, 2005; Heesemann *et al.*, 2006; Matsumoto and Young, 2009). The effector proteins YopE, YopH, YopT, YopJ/P, YopM, and YpkA/YopO are injected and perform different cellular function (Viboud and Bliska, 2005; Heesemann *et al.*, 2006). While YopE, YopH, YopO, and YopT counteract the phagocytosis by macrophages and neutrophils (Viboud and Bliska, 2005), YopJ/P inhibit the cytokine production and induce apoptosis (Orth,

2002; Ruckdeschel, 2002; Aepfelbacher, 2004; Trosky *et al.*, 2008). YopM interacts with the cytoplasmic kinase RSK1 (ribosome protein S6 kinase 1) and PKN2 (protein kinase C-like 2) but so far the relevance of this interaction in *Yersinia* virulence is not known (Hentschke *et al.*, 2010.; McDonald *et al.*, 2003) (Figure 17).

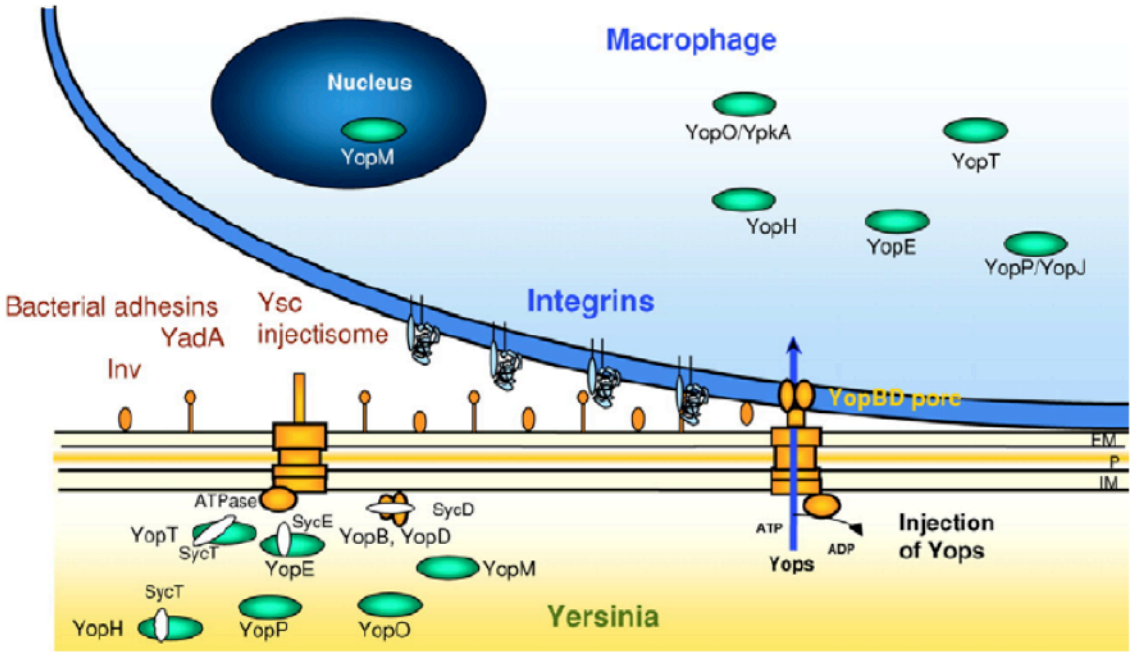


Figure 17: Secretion of the Yop proteins through the type III secretion system (Cornelis, 2002). After colonization of the Peyer's patches *Y. pseudotuberculosis* synthesizes a type III secretion system. Upon cell contact the tip of the needle like structure forms a pore (YopBD) in the membrane of the host cell and Yop proteins are translocated.

1.2.2 Environmental control of virulence gene expression

Three very important environmental signals influence the gen expression of *Y. pseudotuberculosis*: temperature, growth phase and the nutrient availability. All three signals do not only influence the expression of metabolic genes but also strongly influence the expression of virulence factors involved in both the initial and ongoing infection phase. This chapter will introduce the influence of these three signals on some very important virulence factors.

1.2.2.1 Temperature-dependent virulence gene expression

Temperature mediates the expression of adhesin and invasion molecules to ensure, that the invasion factors of the initial infection are produced when the bacteria are taken up by the host and the invasion molecules of the ongoing infection phase are present, when the bacteria reach deeper tissues. *In vitro* InvA expression is highly induced at 25°C while no expression is detectable at 37°C (Nagel *et al.*, 2001). A major regulator of virulence factors of the initial infection phase is the regulator of virulence A (RovA). RovA functions as a thermosensor and in its closed conformation at moderate temperature it has the ability to bind to the genomic region upstream of *invA* activating its transcription. Upon temperature shift to 37°C RovA undergoes a conformational change. The structure opens up and RovA is no longer able to bind to DNA and therefore *invA* expression is reduced (Herbst *et al.*, 2009).
Expression of virulence genes necessary for the ongoing infection is mainly controlled by LcrF. LcrF itself is controlled by the YmoA protein, which binds to the *lcrF* promoter region and inhibiting transcription. At 37°C YmoA becomes susceptible to be degraded by Lon and ClpXP proteases and *lcrF* transcription is induced (Böhme *et al.*, 2012). Similar, the important adhesion molecule YadA, which is necessary in the ongoing infection is not expressed at 25°C while its expression is induced at 37°C (Skurnik and Toivanen, 1992).

1.2.2.2 Growth phase dependent virulence gene expression

The growth phase is also an important stimulus for virulence gene expression. In addition to its temperature dependency, RovA is controlled by the growth phase. In stationary growth a so far unknown factor binds to the RovA protein, which stabilizes it and prevents degradation of the protein by Lon and Clp proteases (Herbst *et al.*, 2009). On the contrary, the expression of the YmoA protein is repressed in the stationary growth phase (Böhme, unpublished).
The cytotoxic necrotizing factor (CNFy) influences the virulence of *Y. pseudotuberculosis*. This factor is necessary for the translocation of Yop proteins into the host cell. In addition to a temperature dependent expression, CNFy expression is also dependent on the growth phase. CNFy expression is induced in the stationary growth phase at both 25°C and 37°C, even though higher protein levels are present at 37°C (Wolters *et al.*, 2013). Additionally, in

Y. pestis a type VI secretion system (T6SS) was reported to be upregulated in stationary growth (Pieper *et al.*, 2009).

1.2.2.3 Nutrient-dependent expression of virulence genes

Similar to temperature and growth phase nutrient availability leads to altered gene expression of metabolic as well as virulence-associated genes. The cAMP receptor protein (Crp) is a very important regulator interconnecting nutrient availability and virulence in *Y. pseudotuberculosis* (Heroven *et al.*, 2012). It binds to the Crp-box consensus sequence TGTGA-N_6-TCACA within the DNA in response to cAMP binding (Gunasekera *et al.*, 1992; Busby and Ebright, 1999). In the presence of glucose Crp and cAMP levels are strongly reduced preventing the bacteria to metabolize other carbon sources. This process is called carbon catabolite repression (Ishizuka *et al.*, 1994). In *Y. pseudotuberculosis* Crp controls the expression of metabolic genes. Additionally, Crp influences CsrC levels signaling down to increased RovA and invasin levels (Heroven *et al.*, 2012). Microarray experiments showed, that deletion of the *crp* gene results in altered gene expression of metabolism associated genes, especially amino acid metabolism and nucleotide metabolism associated genes, and virulence associated genes. Thereby, Crp interconnects metabolism and virulence, to enable the bacteria to efficiently use the available nutrient and, in parallel, to maintain an infection. Similar, deletion of *crp* in *Y. pesits* results in an avirulent phenotype. The plasminogen activator protein Pla promotes dissemination of the bacterium from the periphery to deeper tissues. Deletion of *crp* results in loss of *pla* expression. Further, Crp induces the expression of YopJ and YpkA. In *Y. enterocolitica* deletion of *crp* results in reduced expression of the T3SS and virulence (Petersen and Young, 2002; Kim *et al.*, 2007; Zhan *et al.*, 2008; Zhan *et al.*, 2009).

1.2.3 Impact of regulatory sRNAs on *Yersinia* virulence and other pathogens

In addition to the transcriptional regulation *Y. pseudotuberculosis* and other pathogens have evolved post-transcriptional strategies to fine-tune the expression of virulence factors. In *Y. pseudotuberculosis* the already introduced Csr system plays an important role in

regulating the expression of virulence factors of the initial infection phase. The CsrA protein positively regulates expression/synthesis of RovM by a so far unknown mechanism, which then has a negative effect on *rovA* expression. CsrB and CsrC sequester CsrA influencing its ability to activate *rovM* production and, thereby, the expression of *invA* (Heroven *et al.*, 2008).

The SsrA sRNA together with SmpB is also involved in the regulation of *Y. pseudotuberculosis* virulence. Deletion of these factor resulted in increased sensitivity to stress signals such as oxidative stress. Additionally, lower Yop secretion as well as reduced survival and replication in macrophages and loss of motility have been observed. Further, the deletion mutant showed an avirulent phenotype in the mouse model. Reduced Yop production can be drawn back to reduced LcrF levels (Okan *et al.*, 2006).

The influence of RyhB on *Yersinia* virulence was investigated in *Y. pestis*. RyhB is involved in the iron homeostatis of *E. coli* and *Vibrio cholerae* and is regulated in a Fur dependent manner (Massé and Gottesman, 2002; Davis *et al.*, 2005). When low iron concentrations are present, RyhB acts as a negative regulator and represses the production of iron storing or -using proteins (mechanism see section 1.1.2). *Y. pestis* carries two copies of the RyhB sRNA, which are also present in *Y. pseudotuberculosis*. Deng *et al.*, 2012 showed that RyhB1 is dependent on Hfq, while RyhB2 did not show any Hfq dependency. Further, RyhB1 expression is induced during mouse infection but a mutation of both sRNAs did not have an impact on virulence. In *Neisseria gonorrhoeae* the sRNA NrrF seams to act as an additional iron dependent regulator of gene expression by modulating the mRNA turn over of its targets in response to iron availability (Jackson *et al.*, 2013).

In *E. coli dppA* is a target of the sRNA GcvB. *dppA* encodes a dipeptide-binding protein and its expression is regulated in response to environmental signals (Olson *et al.*, 1991). GcvB binds the SD sequence of the *dppA* mRNA and represses its translation (Sharma *et al.*, 2007; Pulvermacher *et al.*, 2008). The deletion of *gcvB* in *Y. pestis* resulted in changed colony morphology as well as slower growth, which could indicate an impact on its virulence (McArthur *et al.*, 2006).

Koo et al., 2011, identified the sRNAs Ysr29 and Ysr35. Deletion of theses sRNAs resulted in reduced mortality of infected mice, indicating that both sRNAs play an important role in *Yersinia* virulence. Targets of Ysr35 were not yet identified but Ysr29 targets e.g. *ureC, groEL, dnaK* and *ompA*.

The impact of other well-characterized sRNAs on *Yersinia* virulence is not studied, but research in *E. coli* and *Salmonella* hint to an association of some of these sRNAs to virulence. In *E. coli* the sRNA CyaR regulates *ompX*, *nadE,* and *luxS* expression. Binding of CyaR to its target mRNAs overlaps the RBS and results in inhibition of ribosome binding (Papenfort *et al.*, 2008; De Lay and Gottesman, 2009). In *Yersinia ompX* encodes an Ail homologue, which is essential for adhesion to and invasion into epithelial cells and it is necessary for resistance to the bacteriocidal effect of human serum (Kolodziejek *et al.*, 2010). *luxS* encodes for a quorum sensing system and influences biofilm formation (Bobrov *et al.*, 2007). *Y. pestis* requires biofilm formation to colonize the flea and for efficient transmission to the human host. Deletion of *luxS* resulted in higher susceptibility to oxidative stress (Chouikha and Hinnebusch, 2012; Yu *et al.*, 2013). Indeed, in *Bacillus anthracis* LuxS regulates the expression of virulence genes (Jones *et al.*, 2010).

Additionally, in *S. aureus* the sRNA ArtR also regulates *luxS* by direct binding. Simultaneously, ArtR can bind to the 5' UTR of the *sarT* mRNA, which results in increased mRNA degradation. This signals down to reduced α-toxin production and, therefore, has an impact on bacterial virulence (Xue *et al.*, 2013).

In *E. coli* OmrA/B was shown to control the expression of *ompT, cirA, csgD* and *ompR* (Guillier and Gottesman, 2008). *ompT* is a homologue of *pla*, while *cirA* is a homologue of FyuA. In *Y. enterocolitica* FyuA acts as dual receptor for yersiniabactin and the *Y. pestis* bacteriocin pesticin. Deletion of this factor results in reduced bacterial survival in the mouse (Rakin *et al.*, 1994). In *E. coli* CsgD is involved in curli and biofilm formation (Prigent-Combaret *et al.*, 2001; Holmqvist *et al.*, 2010). OmpR regulates *invA* and *flhDC* expression in *Y. enterocolitica, flhDC*, one of the type VI secretion systems, and urease expression are influenced in *Y. pseudotuberculosis* (Flamez *et al.*, 2008; Y Hu *et al.*, 2009; Yangbo Hu *et al.*, 2009; Raczkowska *et al.*, 2011; Brzóstkowska *et al.*, 2012). Therefore, OmrA/B might also be considered to control virulence gene expression.

Recently, in *Salmonella* an sRNA was described, that regulates the expression of the chaperon trigger factor. This factor is associated with ribosomes and important for correct folding of cytosolic proteins. The sRNA SraL has a negative impact on its expression by binding close to the ribosome binding site of its mRNA. Since the trigger factor is well conserved in many bacterial species and plays an important role in the folding of proteins, an impact of SraL on virulence might be possible (Silva *et al.*, 2013).

sRNAs such as RybB, MicA, and MicM regulate outer membrane proteins. Deletion of RybB did not influence *Yersinia* virulence, and its targets are not yet characterized. In *E. coli* MicA binds the SD sequence of its targets and represses the expression of *ompA* and *phoP* (Udekwu *et al.*, 2005; Coornaert *et al.*, 2010). Both genes were reported to be essential for *Yersinia* virulence. Additionally, the *ompX* is repressed in *E. coli*, which was also reported to be necessary for *Yersinia* virulence (Fisher *et al.*, 2007; Kolodziejek *et al.*, 2010; Bartra *et al.*, 2012). MicA, MicM, and OmrA/B were most abundant at 37°C in a deep sequencing approach, indicating a potential influence on *Yersinia* virulence (Koo *et al.*, 2011; Schiano and Lathem, 2012). Indeed, their expression was very high, when mice were infected with *Y. pestis.* Additionally, CyaR, 6S RNA and SsrA levels were very high indicating a potential impact on *Yersinia* virulence (Yan *et al.*, 2013).

Thermosensory elements on the RNA level also influence the expression of virulence factors. In *Y. pseudotuberculosis* LcrF expression is not only dependent on YmoA but also on a RNA thermometer. LcrF is encoded on the virulence plasmid pYV and is transcribed in an operon with *yscW (virG*; located upstream of *lcrF*). At 25°C the mRNA forms a hairpin structure in the intergenic region and the *lcrF* Shine Dalgarno (SD) sequence is captured in a double-stranded region. Ribosome binding is prevented and *lcrF* expression is blocked. At 37°C this structure melts allowing ribosomes to bind and translate the *lcrF* mRNA (Böhme *et al.*, 2012).

Thermosensory elements might also act in concert with other regulatory RNA elements. The regulation of *prfA* expression (positive regulator for listeriolysin) in *L. monocytogenes* is dependent on a thermosensor in its 5’ UTR and two riboswitches that act as *trans* sRNAs. At 37°C the expression of *prfA* is high indicating that the intrisinc thermometer opens up at this temperature, while it is closed at temperatures < 30°C. The two S-adenosylmethionine (SAM) riboswitches SreA and SreB act as *trans* sRNAs and bind to the 5’ UTR of the *prfA* mRNA and inhibit translation. In the absence of these regulators *prfA* is produced and virulence gene expression is induced (Loh *et al.*, 2009; Loh *et al.*, 2012).

In *Neisseria meningitidis* the expression of three virulence genes is regulated by RNA thermometers. CssA is involved in the capsule biosynthesis of the bacterium, while the factor H binding protein (Hbp) recruits the host complement factor H and Lst is necessary for polysaccharide sialylation. The 5’ UTR of all proteins carries an RNA thermometer. In contrast to the *lcrF* and *prfA* thermometer, the thermometer in front of *cssA*, *hbp* and *lst*

mediate a gradual increase over physiologically relevant temperatures (Loh *et al.*, 2013).

Similar, the Hfq protein plays an important role in *Yersinia* virulence. In *Y. pestis* Hfq might be involved in resistance to heat and oxidative stress as well as nutrient limitation and resistance to antibacterial peptides. Further, Hfq seems to be imported throughout the whole life cycle of *Y. pestis*. Deletion of the *hfq* gene completely blocked the ability of the bacteria to form a biofilm in the flea. Additionally, a *Δhfq* mutant resulted in lower survival rates in macrophages and higher phagocytotic events. In the mouse model the Δ*hfq* mutant showed reduced virulence (J Geng *et al.*, 2009; Rempe *et al.*, 2012). Similar experiments were performed in *Y. pseudotuberculosis* indicating an attenuated virulence phenotype. The Δ*hfq* mutant was still able to colonize organs but it was cleared faster and its ability to survive and replicate within lymphatic tissues was reduced. Furthermore, it was shown that the deletion in the *hfq* gene resulted in a higher motility at 26°C and higher sensitivity to oxidative stress. In addition, lower survival in and adherence to macrophages was reported, which could be explained by the finding that Hfq influences the secretion of Yop proteins (Schiano *et al.*, 2010).

These examples indicate that regulatory RNA elements and the RNA chaperon Hfq are important in fine-tuning the expression of virulence-associated genes.

1.3 Aim of the thesis

So far the regulation of gene expression in *Y. pseudotuberculosis* was only addressed for single genes. New technologies such as high-throughput and pyrosequencing allow a global overview on gene expression in all living organisms. In contrast to microarray experiments, these techniques allow a high resolution of gene expression as well as the identification of transcriptional start sites and novel sRNAs. In *Y. pseudotuberculosis* gene expression is strongly dependent on temperature, growth phase and nutrient availability. Since only few is known about the impact of regulatory RNA elements in *Y. pseudotuberculosis*, the primary goal of this study was the identification of novel sRNAs. Additionally, this study aimed at the identification of the temperature, growth phase and Crp-dependent transcriptome. Some of the newly identified sRNAs were verified and analyzed with respect to their expression and

Hfq dependency. Further, the influence of some sRNAs on *Y. pseudotuberculosis* virulence was examined.

Since many sRNAs were dependent on Hfq, the *hfq* gene regulation and its physiological role in *Y. pseudotuberculosis* YPIII was examined.

2 Material and Methods

2.1 Material

2.1.1 Chemicals, buffers, media, and supplements

Chemicals used in this study were produced by Roth (Karlsruhe), Merck (Darmstadt), Roche (Mannheim), Applichem (Darmstadt), Peqlab (Erlangen), BD Bioscience (Franklin Lakes), Otto Norwald (Hamburg), Sigma-Aldrich (Steinheim), Biochrom (Berlin), Gibco (Darmstadt), Oxoid (Basingstoke) and Hartmann Analytic (Braunschweig) if not stated otherwise. Buffer and media were dissolved in H_2O, if not indicated otherwise and autoclaved for 20 min at 121°C. Thermoinstable substances were sterile filtered using Stericups with a pore size of 0.2 µm (Millipore, Darmstadt). All used media are listed below. If the media were used as agar plates 1.5 % agarose/l was added

LB Medium (Luria-Bertani medium) (Sambrook, 2001)

5 g Bacto yeast extract

10 g Bacto tryptone

5 g NaCl

fill up to 1 L with *aqua bidest*

BHI medium (Brain heart infusion medium):

37 g BHI

fill up to 1 L with *aqua bidest*

***Yersinia* selective medium (Oxoid, Basingstoke)**

29 g Yersinia selective agar

fill up to 500 ml with *aqua bidest*

after autoclaving *Yersinia* specific supplements were added

DMEM/F12 medium

Dulbecco's modified eagle medium (DMEM) was mixed 1:1 with HAM's F12 medium, which was prepared as described in Table 1. The carbon source and the mineral salts were prepared as 12 x concentrated solutions while all remaining components were prepared as 6 x concentrated solutions.

Table 1: Composition of the HAM's F12 medium. The carbon source and mineral salts were prepared as 12 x concentrated solutions, all other components were prepared as 6 x concentrated solution. The components were sterile filtered and mixed with H_2O to an unconcentrated solution.

Name	Concentration
Carbon source	
D-glucose x H_2O	11.892 g/l
Na-pyruvate	660 mg/l
Mineral salt 1 (12x)	
NaCl	45.594 g/l
KCl	1.3416 g/l
Na_2HPO_4 x $7H_2O$	1.6078 g/l
$NaHCO_3$	7.056 g/l
Mineral salt 2 (12x)	
$CaCl_2$ x $2H_2O$	264 mg/l
$MgCl_2$ x $6H_2O$	732 mg/l
amino acid (6x)	
L-alanine	54 mg/l
L-arginine x HCl	1.266 g/l
L-asparagine x H_2O	90 mg/l
L-aspartate	79.8 mg/l
L-cysteine x HCl x H_2O	210.77 mg/l
L-glutamine	876 mg/l
L-glutamate	88.2 mg/l
glycine	45 mg/l

Name	Concentration
L-histidine x HCl x H_2O	126 mg/l
L-isoleucine	24 mg/l
L-leucine	78 mg/l
L-lysine x HCl	219 mg/l
L-methionine	26.8 mg/l
L-phenylalanine	30 mg/l
L-proline	207 mg/l
L-serine	63 mg/l
L-threonine	72 mg/l
L-tryptophane	12 mg/l
L-tyrosine	32.4 mg/l
L-valine	11.7 mg/l
Trace elements (6x)	
$FeSO_4$ x 7 H_2O	5.004 mg/l
$CuSO_4$ x 5 H_2O	0.01494 mg/l
$ZnSO_4$ x 7 H_2O	5.178 mg/l
Vitamins (6x)	
biotine	0.0436 mg/l
D-Ca-Pantothenate	2.88 mg/l
folic acid	7.8 mg/l
icotineamide	0.222 mg/l
pyridoxine x HCl	0.372 mg/l
riboflavin	0.228 mg/l
thiamine x HCl	2.04 mg/l
vitamin B_{12}	8.16 mg/l
Remaining components (6x)	
Choline chloride	84 mg/l
myo-inositole	108 mg/l

Name	Concentration
hypoxanthine	24.6 mg/l
thymidine	4.38 mg/l
liponic acid	1.26 mg/l
linoleic acid	0.504 mg/l
putrescine x 2 HCl	0.966 mg/l

To monitor the influence of osmolarity, strains were grown in LB medium without additional NaCl or modified by the addition of 150 mM or 500 mM NaCl, respectively. To identify the influence of pH the medium was either buffered with 0.1 M MES and the pH was adjusted to 5.5 or the medium was buffered with 0.1 M MOPS and the pH was adjusted to 7 and 8.5, respectively. To determine the influence of oxygen availability on the *hfq* expression, LB medium containing 10 mg/l glucose and 0.2 M HEPES was used. To analyze oxidative stress LB medium supplemented with either 1 mM diamide, 50 µM paraquat (starting from time point 0 h) or by the addition of 100 mM H_2O_2 was used.

After autoclaving antibiotics were added to the desired amounts. All antibiotics were available in stock solution. Chloramphenicol was dissolved in 70 % ethanol while carbenicillin and kanamycin were dissolved in water. Antibiotics were stored at -20°C or 4°C. *Yersinia* selective supplements were dissolved according to the manufacturers protocol. Stock solutions and final antibiotic concentrations are listed in Table 2.

Table 2: Antibiotics used in this study.

Name	Concentration stock solution	Final concentration
carbenicillin	100 mg/ml	100 µg/ml
kanamycin	50 mg/ml	50 µg/ml
chloramphenicol	30 mg/ml	30 µg/ml
gentamycin	50 mg/ml	50 µg/ml

2.1.2 Oligonucleotides

All oligonucleotides used in this study are listed in Table 3. Stock solutions of primer had a concentration of 10 µmol/ml if not stated otherwise.

Table 3: Oligonucleotides used in this study. Restriction sites are underlined; homologous sequences to the kanamycin cassette are marked in red. Sequences are indicated in 5'-3' orientation.

Name	Sequence (5'- 3' orientation)	Description
Oligonucleotides used as probes		
II982	CCTACGCATCTGCGTAGGTCGGTGCAAATAAAAAAC GATCTTTGATAC	probe against OmrA/B
II984	CTTTGTGCTTGCGGCACCGACTTAAGACAGATACGG CACCTTACC	probe against YpseC0083
II985	TCGGTTTAGGTGGACGATAGGCACCAGTCTTAGGCA TCATTCGGA	probe against GlmY
II986	GGGAGATTGGGCTAGCCAAGGAGGTGGTTCCTAGT ATTACTTAAC	probe against CyaR
II988	GCCCCCTGGTGTTGGCTAAAATATATTCACAGCAGA CTAACTTTTTCAGC	probe against YpseC0109
II991	CGCCCCGATTGAATAAACAATCAGGGCGACGTTCCA GTAACCATTG	probe against YpseC0125
II992	CAAAATAAAAGTATAACAAATATGGAGCGCAACGC CCATCGCTTGACG	probe against FnrS
II994	GAGCAATGTCGTGCTTTTCTGACCAAAGCCAAAGAC TGCCTGCCT	probe against RyhB
II999	GAGCCGTGCGCTAAAAGTTGGTATTAATGTAGGCTT ATTCAGCCG	probe against RyeB
III2	CCTGGCTGCCCGTACCACGTTTCAAATAAATGAAAC GAGTATGTTG	probe against YpseC0170
III5	CGGGACTACCGGGCTCCTCAATATGGGGACATCAAA GAAAAGCAG	probe against RybB

Name	Sequence (5'- 3' orientation)	Description
III6	GTTATTAAGCACTCACACTCCTTGCGGATAATGTGAGCACCAGC	probe against MicM
III7	GGCCACATCACTGTGGCCAAATTAACATCTCTAATAGAAGGGATG	probe against MicA
III9	CAATAGGCACTCTAAAATCGGCTCTGCGTCATCCCTGGGTTTATG	probe against GlmZ
III19	CATCGCTTCAAACGGTGCATTGGGTAGTTTGATTGATGCTCGCGG	probe against YpseP0011
III25	GCAAACACAACATCACCACCACAAAGCCAAAAGCATTTCAGTACCTG	probe against GcvB
III830	AGCGTTCGTTACCCGTTTGCTTTGCGGCGAATCTTACGGTAA	probe against YpseC0075
IV286	GCCAAGCCCAAATTGTTAGTGCACAACACATATCATATACAAACCCTTAACAAAACC	probe against Ysr19
IV287	CGCCGTTTTCGGCAAGCAACAAATCAATAGAGAGATTGGTTAGCTTGCCTTGC	probe against Ysr18
IV288	CTGAAAATACCCCTATCACAGCCCTCTCACAAATAGGTTCACCTTGC	probe against Ysr17
IV290	CCTGCTTCCCTGCATAAAAATAGCCTTCCATGGGGGCTAGATCC	probe against Ysr12
IV291	GGTTGGCGAACATATTCATCTTCAACGCTAATATCACAAATGCACAAAATCCTACTCCTC	probe against Ysr10
IV389	GTGTAGGGTGTATGCGAGAGTAAAGCAGTTCCTCCCCAAGCG	probe against YpseC0179
IV869	GCCTACGATCTCTCGTAGGCTTCAGACTGCTGACAAACCCCGATGACGC	probe against YpseC0098
IV870	GGGACAAATTTCCCTCGAGCGCCCTGAAATACCTGCTTGATACCCACGTG	probe against YpseC0177
IV872	CTCTTCCCGTTTTTTTGTGCCCAGAAAACCCCCAGCTAGGCTGGGGG	probe against YpseC0201

Name	Sequence (5'- 3' orientation)	Description
IV873	CAAAAAAGCCCACAAGGGACGCGGTGGGCCAAGTAATCAATTTTGGGTGG	probe against YpseC0209
IV876	GTAGGGGTACAGCAGGGATTCTGTCAGAGCTATGTTTCACGTAAATGAACG	probe against YpseC0279
IV877	CACCGCTACAGCAAACCGGCCAGTAAGCCCTAGCGGTGGTATC	probe against YpseC0285
IV878	GACTGGGGCGGCTAATATACAGCCAAATCCGATTACGTGAAGTAAAAGG	probe against Spot42
IV892	GACCTTATAGAACTGATGGAACGTAAAAGCCTCAACCAAACACAGGTTTCACGCG	probe against YpseC0015
IV893	CTTATTGGGTGCTAACCGATAATGGATTTGGCAGCAAAGCTAACTCACCTGATGCC	probe against YpseC0036
IV894	CCCCGACCGAGGCCGGGGTGAGCGAAGACTGCGCCAACACC	probe against SraH
IV895	CAAAAGCGGCCCTGCAAGGCCGCCAATGTAACTACAAAAAACTTAAGCC	probe against YpseC0054
IV896	CAGCGAAGCCCGGAAGTGTCTCACCACTAACCGGGCCTCTTACCACC	probe against YpseC0055
IV897	CGCGTCGGTAGCAGCAACTACCGACGCGTCTAAAAAACCTAACGGAGATAC	probe against YpseC0081
IV898	CAGGATCAGGCAGTGGTGGTCGCCATTAACACTGATCCTGAGCAAGTGGAG	probe against YpseC0162
IV899	GGTCAGAGACCGGTCGTAACATTAACGAACTATCTGACTGTGTTAGCCACAATGATAG	probe against YpseC0190
IV900	CGTTAACGAACAAGAAGCTGCATATGGCACAACAAGTACAACTCAGCGCAACGGTGGC	probe against YpseC0230
IV901	GTGCGCTAACACTAACCGGGCCTCTAACCACCAACGATAGTCAACGTATC	probe against YpseC0293
V351	GGCTACTGTATCATTGCCTACATGTCGAATTTAATTCAG	probe against YPK_transRNA_38

Name	Sequence (5'- 3' orientation)	Description
V352	GCTATTCGACAGATTTCTCATCTCAGTGGGC	probe against Crp2
V353	CGGCGTCTTTACGATCTGCCTGTTCTCTCCGTCG	probe against YPK_transRNA_71
V355	GTTGCTGGATATCCACATTCCAATAAAAAACAATCA AGCCG	probe against YPK_asRNA_30
V357	CGCGGGCACTTTGTCAATAACCTCATCATTATTCCTT TACG	probe against YPK_transRNA_73
V402	CACTGCGATGGCGCCAAATCTACTGGCTGCTGATTT CGCTGC	probe against YPK_asRNA_59
V403	GGCGGATGCTTTCAGTACCAACACCGTCACCCGCGT GATTG	probe against YPK_asRNA_52
V404	CAGCAGAGGGCGATGTGGACATGGATTTCGATATT AAAAATTAGCGGTAC	probe against YPK_asRNA_50
V405	CCTGTTTGCATCAACGGTGCGGTAGCTGTTCCATTCA CCCGAATC	probe against YPK_asRNA_46
V407	CGAACACAGTCCTGTTTATCAAAACGGATGATGCCG ATCATCTCATCCTC	probe against YPK_asRNA_24
V408	GCCAATCCGTCATTTTTTCTCCCCCTCCGATGTTATTA CATAAATATT ATTACATAACCGTTATTGC	probe against YPK_asRNA_23
V409	CCGATTCGGTCCTGAATGTTGGGGCCAACCGAAGTG AAGTTG	probe against YPK_asRNA_12
V411	GACGCGCCCTTGGCTTACGTTAACGAATCGGGGTTC GTTTGC	probe against YPK_asRNA_1
V414	GAGCGTTCGTTACCCGTTTGTCTTGCGGCGAATCTTA CGGTAAC	probe against YPK_transRNA_63
V415	CAGACGTTATCTGTGACTGGAAGCACTAAGTTGTTG GTTAATGGCTCTC	probe against YPK_transRNA_58
V417	GGTGATGGTGATTAAATTGAACGCGATTCATAGTGG CTTCTCTGTTTGGGC	probe against YPK_transRNA_48
V418	GATGATAACGTGCTCGCGATGGAGAGAATAGGCAG AGTAAGTAAAGACG	probe against YPK_transRNA_43

Name	Sequence (5'- 3' orientation)	Description
V420	GGTTTTACGCCGTTGATTTTGTCGCAGCATACGCCAGCGACCAAC	probe against YPK_transRNA_37
V421	CTTTCGCACAACGCCACGCCAGTAGCTGCGCTCAATACATCG	probe against YPK_transRNA_35
Oligonucleotides used to generate promoter upstream regions for bandshift assays		
V358	CAGCAAGGCCACTCGCTC	forward primer to generate promoter fragment of YPK_transRNA_38
V359	CATGGGTTGCTCCTGTAAATATC	reverse primer to generate promoter fragment of YPK_transRNA_38
V360	GCTCATTTATGTGACTTTAATC	forward primer to generate promoter fragment of *crp2*
V361	GCTCATTTATGTGACTTTAATC	reverse primer to generate promoter fragment of *crp2*
V362	CGAAGATTAATCGCCCTGG	forward primer to generate promoter fragment of YPK_transRNA_71
V363	CACATATTGTTAGTTGTTGAAC	reverse primer to generate promoter fragment of YPK_transRNA_71
V366	CTCATACTGCCTTGTCTTATTC	forward primer to generate promoter fragment of YPK_asRNA_30
V367	CGTAATTATTTTCACCTCGG	reverse primer to generate promoter fragment of YPK_asRNA_30
V370	CGTTTGCCGCCTTCCTGTAG	forward primer to generate promoter fragment of *omrA/B*

Name	Sequence (5'- 3' orientation)	Description
V371	GTTGATTATTCACCAATTAATACC	reverse primer to generate promoter fragment of *omrA/B*
V372	CCCTAGAGAGCATGCAGGA	forward primer to generate promoter fragment of *cyaR*
V373	GGACTATACTATCCGACTGC	reverse primer to generate promoter fragment of *cyaR*
V374	GGGATGCAATGTAAACGGAAC	forward primer to generate promoter fragment of *micM*
V375	CACTCCTTGCGGATAATGTGAG	reverse primer to generate promoter fragment of *micM*
V376	GGCACACAGAAGCGTAAATC	forward primer to generate promoter fragment of *micA*
V377	GGGATGATGATAACAAATGCG	reverse primer to generate promoter fragment of *micA*
V378	CGTTGCTGCCAATGTGCCG	forward primer to generate promoter fragment of YPK_transRNA_73
V379	CCTCATCATTATTCCTTTACGG	reverse primer to generate promoter fragment of YPK_transRNA_73
V380	CGCACTATCGTTACTGATGG	forward primer to generate promoter fragment of *gcvB*
V381	GCAGCACCGTTATTTTGGC	reverse primer to generate promoter fragment of *gcvB*
Oligonucleotides used for qRT-PCR		
IV116	GACCGGCCACAACCACCG	qRT-PCR forward primer for *invA*
IV117	CCAGTTGTGGGAGTGCAGG	qRT-PCR reverse primer for *invA*

Name	Sequence (5'- 3' orientation)	Description
IV126	GGCCGTGAGGATGATTGGC	qRT-PCR forward primer for YPK_3388
IV127	CGAAGGTATGCCCTCCCGC	qRT-PCR reverse primer for YPK_3388
IV953	GGGGAAGGTGGAATACATTTCAG	qRT-PCR forward primer for *yopP/J*
IV954	CCACATTCAGATGAGCTTCGC	qRT-PCR reverse primer for *yopP/J*
IV955	GGTAGCGGAGATGGTCAGCG	qRT-PCR forward primer for *yopD*
IV956	CACCAATGTTACTCATTTGCTGC	qRT-PCR reverse primer for *yopD*
IV959	GGAGGGGAGCCATAAACCGG	qRT-PCR forward primer for *yopE*
IV960	GTGATACTGCCACGAAGAGGG	qRT-PCR reverse primer for *yopE*
IV965	GAGGTTTCAACCTGAAGTATCG	qRT-PCR forward primer for *ail*
IV966	GCCTTTCCATGACCTGCCCC	qRT-PCR reverse primer for *ail*
V36	CTTTCTCTCTTAATGGCAAAACCC	qRT-PCR forward primer for YPK_2030
V37	CTCGGTCACCACTTTAGAACCTG	qRT-PCR reverse primer for YPK_2030
V42	GGTTAAAGTTCATCCCAAAGGCC	qRT-PCR forward primer for YPK_3923
V43	GAAGTAGCCTATAAAACCTGTGGCA	qRT-PCR reverse primer for YPK_3923
V46	GGCACCGTCTCTGACGCT	qRT-PCR forward primer for YPK_2072
V47	CGTTTTGCACCGTCAGTTGC	qRT-PCR reverse primer for YPK_2072

Name	Sequence (5'- 3' orientation)	Description
V48	CACGGGATGATTGATCTGTCAG	qRT-PCR forward primer for YPK_4229
V49	GGACGCACAGCTGATTTGC	qRT-PCR reverse primer for YPK_4229
V50	CTCAAATCACCTTATGGCATCCG	qRT-PCR forward primer for YPK_0152
V51	GATCGTCAATTTTCACCTCTTTTGG	qRT-PCR reverse primer for YPK_0152
V83	GTGCGTATGTCACGACCATT	qRT-PCR forward primer for *yscW*
V84	TCCTCGCTCTGGAAAAGAGA	qRT-PCR reverse primer for *yscW*
V153	GCTGGCATGAACGTTATGCG	qRT-PCR forward primer for YPK_1855
V154	CAGTTTCATGGTCCGGATTTCAGG	qRT-PCR reverse primer for YPK_1855
V175	GATGCTGAATGAGCACGAAGTG	qRT-PCR forward primer for YPK_4189
V177	CGTTAATGCCTTTCCAGCCAC	qRT-PCR reverse primer for YPK_4189
V185	CAGAGAACCTTCAGTAGTCTGAG	qRT-PCR forward primer for *fliC*
V186	GCACTGTTGATACGCAGACCG	qRT-PCR reverse primer for *fliC*
V187	GTTCGCCATGAAGCATTGCG	qRT-PCR forward primer for *fliA*
V190	CTGTACCGCATACGTAGTAAAC	qRT-PCR reverse primer for *fliA*
V191	CTTTACTCCAGCGCAACACTG	qRT-PCR forward primer for YPK_3445
V193	CCCATTACCTTGTGGCAATG	qRT-PCR reverse primer for YPK_3445
V261	GCTCAAGTGAATATGGACCTAG	qRT-PCR forward primer for YPK_1985

Name	Sequence (5'- 3' orientation)	Description
V262	GCACGGTTTGCCAGTACCTC	qRT-PCR reverse primer for YPK_1985
V269	GGTATTGGCTTAATGCTAGTGC	qRT-PCR forward primer for YPK_0762
V270	GACGATTATCGCCAGTTCACC	qRT-PCR reverse primer for YPK_0762
V271	CCAAATTGTCCCAGGGCAAC	qRT-PCR forward primer for YPK_1731
V272	CAAAAGGAACGTGGCGTTCAC	qRT-PCR reverse primer for YPK_1731
V273	GGTGACCACTATAAATGGCG	qRT-PCR forward primer for YPK_0554
V274	CAATTCAAGATGCGTCCAATGG	qRT-PCR reverse primer for YPK_0554
V275	CTGTCCGTGCTTAAGGAAAAGG	qRT-PCR forward primer for YPK_2197
V276	GTTGCCTACTTAAGTAAACATGATCTTC	qRT-PCR reverse primer for YPK_2197
V277	GACTAAAAATACTGCGACTAAAGTAAAAAGC	qRT-PCR forward primer for YPK_2200
V277	GAGTGATGACACCCAAACCC	qRT-PCR reverse primer for YPK_2200
V281	GGCAGAAATGAAGGCAGCCTATC	qRT-PCR forward primer for YPK_2676
V282	CAATTTGTTCATATTCCCCTGCC	qRT-PCR reverse primer for YPK_2676
Oligonucleotides used for 5' RACE		
V150	GTAGCATCTTCGCCGCTGAAGCC	SP1 primer for YPK_3761
V151	GATCAACAGCAACACCAGGCG	SP2 primer for YPK_3761
V159	CTCGGACCACTTGTATACCCAAC	SP1 primer for YPK_1918

Name	Sequence (5'- 3' orientation)	Description
V160	CACAACGCAATGCCAGAATTTTAAC	SP2 primer for YPK_1918
V163	GTTAGTTGCCAATTGACGCCAG	SP1 primer for YPK_2676
V164	CTAACATTAGCCCTAAGGAGAAACA	SP2 primer for YPK_2676
V166	CAGAAGCAAAGTGGTTTTTGATCAC	SP1 primer for YPK_2072
V167	CCAGACTCTGTTACAGCCAG	SP2 primer for YPK_2072
V169	CGTTATGCACGACGGAGATATAG	SP1 primer for YPK_4229
V170	GTGCCACCGTGTAAATCCTGC	SP2 primer for YPK_4229
V172	GGTCATACAAGAACAAGCCGG	SP1 primer for YPK_0152
V173	GAATGCGATATGCGGTGCCAG	SP2 primer for YPK_0152
V180	CAGCGGCAATGCGCAAACC	SP1 primer for YPK_2650
V181	GCACCGAACAGCAGTTCTTGG	SP2 primer for YPK_2650
V184	CATCCTGAATAGAGTCCAGGTC	SP1 primer for *fliC*
V185	CAGAGAACCTTCAGTAGTCTGAG	SP2 primer for *fliC*
V188	CAATATCAAGAACCTGCGCGACTTC	SP1 primer for *fliA*
V189	CACTGCGAGGTGCCCAATCAC	SP2 primer for *fliA*
V192	CATGCAGATGGAAACCGTGAATTC	SP1 primer for YPK_3445
V193	CCCATTACCTTGTGGCAATG	SP2 primer for YPK_3445

Oligonucleotides used to generate mutagenesis plasmids

I666	GAAGCAGCTCCAGCCTACACCTATATTTTCCTTATTTGCTTGTTG	reverse primer of upstream fragment to mutate *hfq*
I667	GACTAAGGAGGATATTCATATGGCCCATTGCTGGTCGACC	forward primer of downstream fragment to mutagenize *hfq*
III949	CCGGCCGAGCTCCCCAGTGCGATCAATCACCC	reverse primer of downstream fragment to mutagenize *hfq* generating *Sac*I site
III950	CCGGCCGAGCTCCCAATTTGCGATTGCGCCTG	forward primer of upstream fragment to mutate *hfq* generating *Sac*I site

Name	Sequence (5'- 3' orientation)	Description
Oligonucleotides used to generate promoter fragments and complementation plasmids		
III441	GGCGCGGGATCCAATCACGGTGGGTAGGCGT	forward primer to generate a promoter *lacZ* fusion of the *micM* upstream region producing a *Bam*HI site
III442	GGCGCGGTCGACCCAGCATAGGGTACCAACC	reverse primer to generate a promoter *lacZ* fusion of the *micM* upstream region producing a *Sal*I site
III444	GGCGCGGGATCCCGTGCCAACCACCCTACTT	forward primer to generate a promoter *lacZ* fusion of the *rybB* upstream region producing a *Bam*HI site
III445	GGCGCGGTCGACGCAGTGGCATTAATTCAGACC	reverse primer to generate a promoter *lacZ* fusion of the *rybB* upstream region producing a *Sal*I site
III452	GGCGCGGGATCCGTTATGGCCCATGGTGCG	forward primer to generate a promoter *lacZ* fusion of the YpseC0170 upstream region producing a *Bam*HI site
III453	GGCGCGGTCGACCCCATGAACGGCGCAACC	reverse primer to generate a promoter *lacZ* fusion of the YpseC0170 upstream region producing a *Sal*I site
III461	GGCGCGGGATCCCGAAGATATATGGCCCCAC	forward primer to generate a promoter *lacZ* fusion of the *fnrS* upstream region producing a *Bam*HI site

Name	Sequence (5'- 3' orientation)	Description
III462	GGCGCGGTCGACCACCTGCAAAATAATCATGCC	reverse primer to generate a promoter *lacZ* fusion of the *fnrS* upstream region producing a *Sal*I site
III464	GGCGCGGGATCCGACAAATCCGCGCTGACG	forward primer to generate a promoter *lacZ* fusion of the *ryhB* upstream region producing a *Bam*HI site
III465	GGCGCGGTCGACCGCATCAAAATGATAATACTTATC	reverse primer to generate a promoter *lacZ* fusion of the *ryhB* upstream region producing a *Sal*I site
III466	GGCGCGGGATCCCCGTTTCAGGTATTGGGAG	forward primer to generate a promoter *lacZ* fusion of the YpseC0125 upstream region producing a *Bam*HI site
III467	GGCGCGGTCGACCCTGTAGAAATAGCAATACACC	reverse primer to generate a promoter *lacZ* fusion of the YpseC0125 upstream region producing a *Sal*I site
III478	GGCGCGGGATCCGCTCGGTGCGTGTAACGTC	forward primer to generate a promoter *lacZ* fusion of the YpseC0083 upstream region producing a *Bam*HI site
III479	GGCGCGGTCGACCCTTACCTACTTATCATTGCTC	reverse primer to generate a promoter *lacZ* fusion of the YpseC0083 upstream region producing a *Sal*I site

Name	Sequence (5'- 3' orientation)	Description
III497	GGCGCGGGATCCGAAACCCCGCAATGCGGG	forward primer to generate a promoter *lacZ* fusion of the *glmZ* upstream region producing a *Bam*HI site
III498	GGCGCGGTCGACGCATCTACAGGTTAGATATTGC	reverse primer to generate a promoter *lacZ* fusion of the *glmZ* region producing a *Sal*I site
III500	GGCGCGGGATCCCGTTTGCATCAATGAACGCTTG	forward primer to generate a promoter *lacZ* fusion of the *glmY* upstream region producing a *Bam*HI site
III501	GGCGCGGTCGACGCAACTGTTATTGATAATGCAG	reverse primer to generate a promoter *lacZ* fusion of the *glmY* upstream region producing a *Sal*I site
IV906	GGCGCGGGATCCCTCGTAAACAGGCTGCTGAGC	forward primer to generate a promoter *lacZ* fusion of the *spot42* upstream region producing a *Bam*HI site
IV907	GGCGCGGTCGACCCCTACGTCTATAACTCTACATC	reverse primer to generate a promoter *lacZ* fusion of the *spot42* upstream region producing a *Sal*I site
IV910	GGCGCGGGATCCGTAAACGGGCTACCGGGATAC	forward primer to generate a promoter *lacZ* fusion of the YpseC0201 upstream region producing a *Bam*HI site

Name	Sequence (5'- 3' orientation)	Description
IV911	GGCGCGGTCGACGTTAAAACAGTTTGCGGTCTGGC	reverse primer to generate a promoter *lacZ* fusion of the YpseC0201 upstream region producing a *Sal*I site
V71	GCGCCGGGATCCCAATTTGCGATTGCGCCTGC	forward primer to generate a promoter *lacZ* fusion of the *hfq* upstream region starting from position -305 producing a *Bam*HI site
V72	GCGCCGGTCGACCGGAACCCGTTCACGACGCAA	reverse primer to generate a translational promoter *lacZ* fusion of the *hfq* upstream region up to position +63 producing a *Sal*I site
V75	GCGCCGGGATCCGATATCCGTGATCCCGCTGAATC	forward primer to generate a promoter *lacZ* fusion of the *hfq* upstream region starting from position -716 producing a *Bam*HI site
Oligonucleotides used for sequencing		
350	GGGTTTTCCCAGTCACGACG	sequencing primer binding in *lacZ*
I984	TAAGAAACCATTATTATCATGAC	sequencing primer for pFU series, binds in P1-site
III981	TGAACGGCAGGTATATGTG	sequencing primer for pAKH3
III982	CACTTAACGGCTGACATGG	sequencing primer for pAKH3
V477	TCACACAGGAAACAGCTATGAC	M13 reverse sequencing primer

2.1.3 Strains and plasmids

All strains and plasmids are listed in Table 4.

Table 4: Strains and plasmids used in this study.

Name	Description	Reference/Source/Primer for construction
***E. coli* strains**		
DH10β	F- *mcrA* Δ(*mrr-hsd*RMS-*mcr*BC) Φ80d*lacZ*ΔM15 Δ*lac*X74 *endA1 recA1 deoR* Δ(*ara*, *leu*)7697 *ara*D139 *galU galK nup*G *rpsL* λ-	(Casadaban and Cohen, 1980)
S17 1 λ pir	*recA thi pro hsdR* – M1+ (RP4-2 Tc::Mu-Km::Tn7), λ pir	(Simon *et al.*, 1983)
CC118 λ pir	F- Δ(*ara-leu*) 7697 Δ(*lacZ*)74 Δ(*phoA*)20 *araD139 galE galK thi rpsE rpoB arfEam recA1,* λ *pir*	(Manoil and Beckwith, 1986)
***Y. pseudotuberculosis* strains**		
YPIII	pIB1, wild type	(Bolin *et al.*, 1982)
YP80	pIB1, Δ*hfq*	(Heroven *et al.*, 2012)
YP89	pIB1, Δ*crp*	(Heroven *et al.*, 2012)
IP32953	pYV^+, wild type	(Chain *et al.*, 2004)
YPIP05	pYV^+, Δ*hfq*	This study
YPIP09	pYV^+, *micA::kan*	Heroven, unpublished
YPIP11	pYV^+ *cyaR*-sRNA::*kan*	Heroven, unpublished
Plasmids		
pAKH03	pCP704, sacB+, Amp^R	(Heroven *et al.*, 2012)
pAKH36	pACYC184-*crp*, p15A, Cm^R	(Heroven *et al.*, 2012)
pAKH56	pACYC184-*csrA*, p15A, Cm^R	(Heroven *et al.*, 2008)
pBW33	Amp^R, $P_{YpseC0201}$::rbs-*lacZ*, ori29807	This study/primer IV910, IV911

Name	Description	Reference/Source/Primer for construction
pBW35	Amp^R, P_{spot42}::rbs-*lacZ*, ori29807	This study/ primer IV906, IV907
pBW46	Amp^R, rbs-*lacZ*, ori29807	This study/ fragment got from (Uliczka *et al.*, 2011)
pBW88	Amp^R, P_{ryhb}::rbs-*lacZ*, ori29807	This study/ primer III464, III465
pBW90	Amp^R, $P_{YpseC0083}$::rbs-*lacZ*, ori29807	This study/ primer III478, III479
pBW99	Amp^R, $P_{YpseC0170}$::rbs-*lacZ*, ori29807	This study/ primer III452, III453
pBW105	Amp^R, P_{fnrS}::rbs-*lacZ*, ori29807	This study/ primer III461, III462
pBW107	Amp^R, $P_{YpseC0125}$::rbs-*lacZ*, ori29807	This study/ primer III466, III467
pBW109	Amp^R, $P_{YpseC0212}$::rbs-*lacZ*, ori29807	This study/ primer III441, III442
pBW125	pCP704, sacB+, Amp^R, Kan^R, hfq_{up}::*kan*::hfq_{down}	This study/ primer I668, I667, I666, I669
pBW131	Cloning vector, $SC101^*$, P_{lac}, Cm^R, *hfq*+	This study/ primer V75, V80
pBW137	Amp^R, P_{hfq2+3}::rbs_{hfq}-*lacZ*, ori29807	This study/ primer V72, V75
pBW138	Amp^R, P_{hfq3}::rbs_{hfq}-*lacZ*, ori29807	This study/ primer V71, V72
pACYC184	Cloning vector, p15A, Cm^R, Tet^R	(Chang and Cohen, 1978)
pCP20	FLP recombinase expression vector, Amp^R, Cm^R	(Datsenko and Wanner, 2000)
pDrive	Amp^R	Qiagen PCR Cloning Kit (Qiagen, Hilden)
pFU62	Amp^R, rbs-*lacZ*, ColE1 (*Sac*I-site removed)	(Uliczka *et al.*, 2011)
pFU67	Amp^R, *lacZ*, $SC101^*$	(Uliczka *et al.*, 2011)
pHSG575	Cloning vector, $SC101^*$, P_{lac}, Cm^R	(Takeshita *et al.*, 1987)

2.2 Methods

2.2.1 Microbiological Methods

2.2.1.1 Cultivation of *E. coli* and *Y. pseudotuberculosis*

Y. pseudotuberculosis and *E. coli* cultures were cultivated under aerobic conditions either in solid or in liquid medium. *E. coli* was mainly cultivated at 37°C, while *Y. pseudotuberculosis* cultures were incubated both at 25°C and 37°C. For liquid cultivation the bacterial cultures were shaken at 200 rpm using a Multitron standard shaker (Infors HAT, Basel).

1.1.1.1. Measurement of cell density and characterization of bacterial growth

The cell density of bacterial cultures was determined by measuring the optical density OD_{600} using the UV/VIS Ultrosprec 2100 pro spectrophotometer (Amersham Bioscience, Chalfont St. Giles). An OD_{600} equivalent of 1 corresponds to 1 x 10^9 cells/ml (Sambrook, 2001) containing 150 µg protein (Miller, 1992). The growth rate and doubling time was calculated using the following formula:

$$\text{Growth rate } [h^{-1}] = \Delta t / \text{ doubling time}$$

$$\text{Doubling time [h]} = 3.3 \times (\log OD_{600}\ t_1 - \log OD_{600}\ t_0)$$

2.2.1.2 Storage of bacterial strains

Bacterial strains streaked on agarose plates were stored at 4°C. For long term storage 1.25 ml bacterial culture were mixed with 750 µl 80 % glycerole and stored at -80°C.

2.2.2 DNA methods

2.2.2.1 Isolation of genomic and plasmid DNA

Plasmid DNA was isolated using the QIAprep Spin Miniprep Kit (Qiagen, Hilden) according to the manufacturers protocol.

To isolate chromosomal DNA 2 ml of an over night culture were spun down. Subsequently, the pellet was resuspended in 350 µl resuspension buffer (50 mM Tris-HCl pH 8.0, 50 mM EDTA pH 8.0) and mixed with 20 µl 10 % SDS and 100 µl pronase solution (10 mg/ml). The mixture was incubated for 1 h at 45°C until it became clear (extend incubation time if necessary). Afterwards the solution was mixed with 150 µl phenol, incubated for another 1 h at 37°C and inverted occasionally. After the addition of 600 µl chloroform and a vortex step for 5 sec centrifugation was performed in a tabletop centrifuge at max. speed for 15 min. The aqueous phase was then transferred into a new reaction tube and the DNA was precipitated using 60 µl 3 M NaOAc and 300 µl 96 % ice cold EtOH. After carefully inverting, the DNA was again transferred into a new reaction tube and washed twice with 96 % ice cold EtOH. Subsequently, the DNA was resuspended in 400 µl TE buffer (10 mM Tris-HCl pH 8.0, 1 mM EDTA pH 8.0) and 20 µl RNase were added and incubated for 1 h at 37°C. Subsequent DNA precipitation was carried out with 40 µl 3 M NaOAc and 400 µl 96 % EtOH overnight at -20°C. The DNA was collected for 30 min at 4°C and washed twice in 70 % EtOH. The pellet was resuspended in 200 µl H_2O.

To isolate DNA with a specific size out of a pool of different fragments DNA was size separated by agarose gel electrophoresis (see 2.2.2.5) and bands with the size of interest were isolated from the gel. Isolation was carried out using the QIAquick Gel Extraction Kit (Qiagen, Hilden). To isolate DNA from polyacrylamide gels, the corresponding bands were isolated from the gel and the gel slice was incubated in a shaker in 400 µl elution buffer (100 mM NaOAc, 0.5 % SDS, 10 mM EDTA) for 1.5 h at RT. The liquid was then collected and the gel slice was incubated for another 1.5 h in 400 µl elution buffer. The eluate was then mixed with three volumes 96 % EtOH and 1/10 Volume 3 M NaOAc pH 5.6. After incubation over night at -20°C the precipitated DNA was pelleted for 30 min at 4°C and 12,000 rpm (Microcentrifuge 5415 R, Eppendorf, Hamburg) and washed in 75 % EtOH. Finally, the DNA pellet was resuspended in 50 µl H_2O.

2.2.2.2 Polymerase chain reaction (PCR)

Polymerase chain reaction enables to amplify specific DNA fragments *in vitro.* The method uses two oligonucleotides binding at the 5' and 3' end of the DNA fragment of interest and a polymerase synthesizes the complementary strain. Oligonucleotides used in this study are listed in Table 3. The annealing temperature was calculated using the following formula:

Annealing Temperature [°C] = (no. of G/C * 4°C + no. of A/T * 2°C) – 4°C

Pfu DNA polymerase (Fermentas, St. Leon-Rot), *Taq* DNA polymerase (NEB, Ipswich), LongAmp® *Taq* polymerase (NEB, Ipswich), and MangoMix (Bioline, London) were used according to manufacturers protocol. Either chromosomal or plasmid DNA was used as template. The reaction was carried out either in a thermocyler T3000 (Biometra, Göttingen) or in a Mastercycler personal (Eppendorf, Hamburg). A characteristic PCR program is listed below (Table 5).

Table 5: PCR Program

	Temperature	**Time**	**No. of cycles**
Initial denaturation	95°C	5 min	1x
Denaturation	95°C	1 min	30x
Annealing	variable	30 s	30x
Extension	72°C (*Pfu*, *Taq*, Mango-Mix), 68°C (LongAmp)	1 kb/min (*Taq*, LongAmp, MangoMix), 2kb/min (*Pfu*)	30x
Final extension	72°C (*Pfu*, *Taq*, Mango-Mix), 68°C (LongAmp)	5 min	1x
Pause	15°C		

2.2.2.3 Colony PCR

This method was used to directly analyze, if a plasmid or a bacterial strain contained the fragment of interest using a bacterial colony as template. Therefore, a bacterial colony was resuspended in 10 µl H_2O (*bidest*) and 5 µl were taken to inoculate either 5 ml LB medium for plasmid isolation or spotted on a LB agar plate. Both media contained the selective antibiotics. The resuspended bacteria were incubated in H_2O for at least 10 min to lyse the

cells. Subsequently, 1 µl was used as template in a PCR reaction. An exemplary reaction mix is listed below.

Reaction mix:	12.5 µl MangoMix (Bioline, England)
	0.75 µl primer 1
	0.75 µl primer 2
	10 µl H_2O
	1 µl template
	Σ 25 µl

2.2.2.4 Sequencing

Sequencing was performed at the in house facility of the Helmholtz Center for Infection Research using the Sanger method (Sanger *et al.*, 1977).

2.2.2.5 Agarose gel electrophoresis

To separate DNA fragments of different length agarose gel electrophoresis was used. Depending on the expected fragment size and the approach 0.8 %, 1.5 % or 2 % gels were used in 1 x TAE (40 mM Tris, 2 mM EDTA, pH 8.0). For smaller fragments 0.5 x TBE gels were used (45 mM Tris-HCl, 44.5 mM boric acid, 1.25 mM EDTA pH 8.0). Samples were mixed with 5 x loading dye (Fermentas, St. Leon-Rot) and as a size standard the GeneRuler^{TM} 100 bp DNA Ladder (Fermentas, St. Leon-Rot) was used (Figure 18). Typically, electrophoresis was carried out for 45 min at 120 V. To visualize DNA fragments, the gels were stained in ethidium bromide. Detection was performed using the Gel Doc XR System (BioRad, München) exposing the gels to UV light at 254 nm. For isolation of DNA from agarose gels, a wavelength of 366 nm was used to reduce the mutation rate.

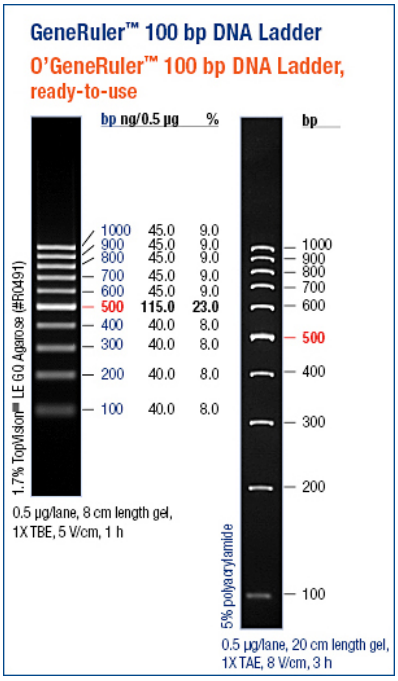


Figure 18: DNA size standard for agarose gel electrophoresis (Fermentas, St. Leon-Rot).

2.2.2.6 Cloning techniques

2.2.2.6.1 Digestion of DNA

Digestion of DNA was used to generate overhangs with a specific sequence to integrate, e.g. PCR products into a vector. Therefore, type II restriction enzymes were used. Enzymes and buffers were delivered by New England Biolabs (Ipswich) and digestion was carried out for at least 60 min at the optimum temperature as described by the manufacturer. Digested plasmids were size fractionated by agarose gel electrophoresis (2.2.2.5) and subsequently isolated by agarose gel extraction. Smaller fragments were directly purified using the QIAquick PCR Purification Kit (Qiagen, Hilden).

2.2.2.6.2 Dephosphorylation of DNA

To reduce religation of plasmid DNA in a ligation reaction, plasmids were dephosphorylated at their 5' ends. In this study, the antarctic phosphatase (NEB, Ipswich) was used according to manufacturers information.

2.2.2.6.3 DNA ligation

For plasmid construction, DNA fragments were ligated into a vector backbone. The T4 DNA ligase (Promega, Mannheim) was used to form new phosphodiester bonds between the insert and the linearized vector. The reaction was carried out as described by the manufacturer.

2.2.2.7 Transformation

2.2.2.7.1 Transformation of *E. coli*

Transformation of electrocompetent *E. coli*

To generate electrocompetent *E. coli* cells, an overnight culture was diluted 1:100 in fresh LB medium and incubated at 37°C until it reached an OD_{600} of 0.5 to 0.8. The cells were chilled on ice for 10-30 min and harvested for 5 min at 600 rpm and 4°C (Sigma 3-18 K centrifuge using 19776-H rotor). Subsequently, the bacterial pellet was first washed with 1/5 volume ice cold H_2O *bidest* and in a second washing step with 10 % glycerol. Finally, the pellet was resuspended in 1/500 volume 10 % glycerol and 40 µl aliquots were used for transformation. For long-term storage, the cells were aliquoted and stored at -80°C.

The electrocompetent *E. coli* were mixed with 1-4 µl plasmid DNA or 10 µl of a dialyzed ligation reaction. The mixture was filled into electroporation cuvettes (electrode gap size of 0.2 mm, Peqlab, Erlangen) and a voltage of 2.2 kV with a capacity of 25 µF and a resistance of 200 Ω was applied. Bacterial cells were supplied with 1 ml BHI medium and incubated at

37°C for 1 h. Afterwards, the cells were streaked on LB agar plates containing the selective antibiotic.

Transformation of chemocompetent *E. coli*

An overnight culture of *E. coli* was diluted 1:100 in LB medium containing 20 mM $MgSO_4$. After incubation at 37°C until the bacteria reached an OD_{600} of 0.5 to 0.8, the cells were harvested as described above and carefully resuspended in 0.4 volume transformation buffer I (30 mM KAc, 10 mM $CaCl_2$, 50 mM $MnCl_2$, 100 mM RbCl, 15 % glycerol). After a second centrifugation step, the cells were washed with transformation buffer II (10 mM MOPS, 75 mM $CaCl_2$, 10 mM RbCl, 15 % glycerol) and finally resuspended in 1/25 volume of transformation buffer II.

For transformation, 100 µl competent cells were mixed with 1-4 µl plasmid DNA or 10 µl of a ligation reaction. The mixture was incubated on ice for 10 min and a heat shock was performed at 42°C for 90 sec. After a second incubation step on ice for 10 min, the cells were supplied with 1 ml BHI medium and incubated for 1 h at 37°C. Finally, the cells were streaked on LB agar plates containing the selective antibiotic.

2.2.2.7.2 Transformation of *Y. pseudotuberculosis*

For transformation *Y. pseudotuberculosis* electrocompetent cells were produced. Therefore, an overnight culture was diluted 1:50 in BHI medium. The cells were grown a 25°C until they reached an OD_{600} of approx. 0.6. Afterwards, the cells were chilled on ice for 10-30 min and subsequently centrifuged at 4°C and 6000 rpm (Sigma 3-18 K centrifuge using 19776-H rotor) for 5 min. The bacterial pellet was washed twice with 1/5 volume transformation buffer (272 mM sucrose, 15 % glycerol) and subsequently resuspended in 1/500 volume transformation buffer. For electroporation, 40 µl competent cells were mixed with 1-4 µl plasmid DNA. The mixture was filled into electroporation cuvettes (electrode gap size of 0.2 mm, Peqlab, Erlangen) and a voltage of 2.2 kV with a capacity of 25 µF and a resistance of 200 Ω was applied. After purchasing the pulse, the cells were resuspended in 1 ml BHI medium and incubated at 25°C for 2 h. Subsequently, the bacteria were plated on LB agar plates containing the selective antibiotic.

2.2.2.8 Mutagenesis of *Y. pseudotuberculosis*

Gene knockouts of *Y. pseudotuberculosis* were generated using homologous recombination. Therefore, fragments of 500 bp length of the upstream and downstream or downstream region of the gene, which should be deleted carrying overlaps to a kanamycin cassette, were amplified by PCR followed by gel extraction. In a second PCR using the kanamycin cassette as well as the upstream and downstream fragment as templates and the flanking primer pair for amplification, one long fragment containing the upstream region, the kanamycin cassette and the downstream region was generated. This fragment was digested with *Sac*I and cloned into the vector pAKH03. This plasmid contains a suicide origin of replication (ori, R6K), which forces *Y. pseudotuberculosis* to incorporate the plasmid into its chromosome in order to survive on selective antibiotics. The mutagenesis plasmid was transformed into *E. coli* S17 1 λ pir. To determine positive clones, colony PCR was performed and the plasmid was isolated and sent for sequencing. Correct clones were subsequently used for conjugation with *Y. pseudotuberculosis* to transfer the plasmid. Therefore, an overnight culture of the *E. coli* strains carrying the plasmid of interest was diluted 1:100 in BHI and incubated for 2.5 h at 37°C in a shaker and 30 min without shaking. In parallel, a *Y. pseudotuberculosis* culture was diluted 1:50 and incubated at 25°C for 3 h. Subsequently, 1 ml of the *E. coli* culture and 4 ml of the *Y. pseudotuberculosis* culture were mixed on a filter and incubated over night on LB plates. After plating the bacteria on *Yersinia* selective agar containing kanamycin single colonies were restreaked on 10 % sucrose plates to remove the plasmid backbone. The plasmid contains the *sacB* gene, which codes for a protein that produces a toxic substance when grown on sucrose. Therefore, the bacteria are only able to grow on this medium after deletion of the *sacB* gene. Selection of positive clones was carried out by colony PCR. These clones were then transformed with the plasmid pCP20 to remove the kanamycin cassette via FRT sites and the FLP recombinase. Afterwards, loss of pCP20 was induced by growth of *Y. pseudotuberculosis* at 37°C, since the plasmid contains a thermosensitive origin. Selection of clones that lost pCP20 and the kanamycin cassette was carried out by growth on LB plates containing no antibiotics, carbenicillin or kanamycin.

2.2.3 RNA methods

2.2.3.1 Isolation of total RNA

The isolation of total RNA for northern blotting was carried out using the SV total RNA Isolation System (Promega, Mannheim). 2 ml of bacterial culture grown at 25°C or 37°C over night or until they reach an OD_{600} of 0.6 – 0.8 (normally after 4 h) were spun down and the pellet was resuspended in 1/5 volume phenol/ethanol mixture (95 % EtOH, 5 % phenol) and snap frozen in liquid nitrogen. The bacterial cells were then lysed using 200 µl TE-lysozyme mix (TE buffer: 100 mM Tris-HCl pH 7.5, 1 mM EDTA pH 8.0, 50 mg/ml lysozyme) and the protocol was further carried on as described by the manufacturer. After purification the amount of RNA was measured at 260 nm using a NanoDrop (Peqlab, Erlangen).

For qRT-PCR and 5' RACE the total RNA was isolated by the hot phenol method. Bacteria were grown to either exponential or stationary growth and 25 ml or 10 ml, respectively, were spun down. The pellets were resuspended in 250 µl resuspension buffer (0.3 M sucrose, 0.01 M NaOAc pH 4.5) and 250 µl 2 % SDS in 0.01 M NaOAc pH 4.5 were added. The mixture was incubated at 65°C for 3 min and snap frozen in liquid nitrogen for 30 sec. After a centrifugation step at 13,000 rpm (Microcentrifuge 5415 R, Eppendorf, Hamburg) for 10 min the aqueous phase was transferred into a new tube and this step was repeated two times. Subsequently, 300 µl chloroform:isoamylalcohol (24:1) were added, the reaction was vortexed for 30 sec and spun down for 3 min in a tabletop centrifuge at full speed. This step was repeated once. Afterwards the RNA was precipitated with 1/10 Vol 3 M NaOAc pH 4.5 and 2.5 volume 96 % EtOH at -20°C over night. After pelleting at 4°C for 30 min the pellet was washed once with 70 % EtOH and resuspended in 50 µl water. To remove remaining DNA fragments, 50 µg total RNA were incubated with 4 U Turbo DNaseI (Ambion, Kaufungen) for 60 min at 37°C. Subsequently, 300 µl phenol:chloroform:isoamylalcohol were added, the mixture was vortexed and separated by centrifugation. Further RNA purification was performed as described above starting with the addition of chloroform:isoamylalcohol.

2.2.3.2 Northern blot analysis

For northern blotting, 10 µg total RNA was loaded onto 7 M urea/ 10 % acrylamide/ 0.6 x TBE (54 mM Tris-HCl, 53 mM boric acid, 1.5 mM EDTA pH 8.0) gels and size separated at 140 V in vertical electrophoresis chambers (Mini-Protean II, BioRad, München). The gels were stained with ethidium bromide and detected as described for agarose gels to determine loading controls. As size standard the RiboRuler™ Low Range RNA Ladder was used (Figure 19).

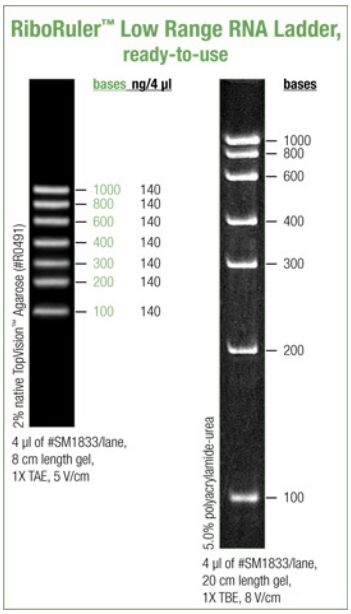


Figure 19: The RiboRuler™ Low Range RNA Ladder was used as size standard in northern blot experiments (Fermentas, St. Leon-Rot).

Subsequently, the RNA was transferred onto a positively charged nylon membrane (Roche, Mannheim) by semi dry blotting at 20 V for 30 min using the TransBlot® SD Semi-Dry Transfer Cell (BioRad, München) in 1 x TBE (90 mM Tris-HCl, 89 mM boric acid, 2.5 mM EDTA pH 8.0). After UV crosslinking the blots were then prehybridized in hybridization buffer (0.5 M Na_2HPO_4, pH 7.2, 1 mM EDTA pH 7.5, 7 % [w/v] SDS) at 65°C for at least 1 h. For radioactive labeling 20 µCi γ-ATP^{32} (Hartmann Analytic, Braunschweig) were mixed with 10 U T4 polynucleotide kinase (Fermentas, St Leon-Rot) and 20 pMol oligonucleotide and incubated at 37°C for 1 h. The reaction was stopped by the addition of STE buffer (100 mM NaCl, 10 mM Tris, pH 8.0, 1 mM EDTA) and the labeled oligonucleotides were purified using

MicroSpin G-25 columns (GE Healthcare, Chalfont St Giles). Probes were mixed with 500 µg yeast tRNA (Invitrogen, Carlsbad) and 250 µg salmon sperm DNA (Invitrogen, Carlsbad) to reduce unspecific probe binding. Denaturation was carried out for 10 min at 95°C. Following hybridization in hybridization buffer over night, the blots were washed twice for 3 min in washing buffer (40 mM Na_2HPO4, pH 7.2, 1 mM EDTA, pH 7.5, 1 % [w/v] SDS) and exposed to a storage phosphor screen (GE Healthcare, Chalfont St Giles). Detection was performed using the Typhoon FLA-9000 (GE Healthcare, Chalfont St Giles).

2.2.3.3 5' RACE

To detect transcriptional start sites, 5' RACE was carried out using the 5'/3' RACE Kit, 2nd Generation (Roche, Mannheim). 1 µg total RNA was used as template and the reaction was carried out as described by the manufacturer. Subsequently, the PCR products were cloned into the vector pDrive using the Qiagen PCR cloning Kit (Qiagen, Hilden). After transformation into *E. coli* DH10β, the plasmids were purified and sent for sequencing as described above.

2.2.3.4 Quantitative real time PCR (qRT-PCR)

To validate the expression of specific genes, qRT-PCR was performed. 1 ng/µl total RNA was used as template for cDNA synthesis and subsequently, the cDNA was used as template for qRT-PCR. The SensiFast™ SYBR No-ROX One Step Kit (Bioline, Luckenwalde) was used according to manufacturers instruction. To determine the optimal annealing temperature, gradient PCR was carried out. All primers used in the study had an optimal annealing temperature of 58°C.

The fold changes was calculated as described previously (Pfaffl, 2001). Therefore, the primer efficiency had to be determined. 1:2 dilutions of genomic DNA were used as template. Primers are indicated in Table 3 and the primer efficiency is listed in Table 6.

Table 6: Primer efficiency determined for primer pairs amplifying the indicated gene products.

Gene	Primer efficiency
YPK_0152	2.22
YPK_1855	1.91
YPK_1918	2.06
YPK_1985	2.12
YPK_2030	2.21
YPK_2072	2.03
YPK_2650	2.08
YPK_2677	2.06
YPK_3388	2.4
YPK_3445	1.91
YPK_3671	2.23
YPK_3923	2.17
YPK_4189	2.02
YPK_4229	2.21
ail	2.15
csrB	2.05
csrC	2.09
fliA	1.91
flhD	1.91
invA	2.1
yopD	2.2
yopE	2.07
yopP/J	1.89
yscW	2.3
YPK_0762	2.33
YPK_1731	2.17
YPK_0554	2.15
YPK_2197	2.19
YPK_2200	2.1

Gene	Primer efficiency
5 S rRNA	2.22
crp	1.99
cyaA	1.97

2.2.4 Biochemical methods

2.2.4.1 β- galactosidase activity assay

To monitor the promoter activity of genes β- galactosidase activity assays were performed. Therefore, promoter fusions of the promoter region of the gene of interest to the *lacZ* gene were constructed and the specific activity was measured using a modified protocol as described previously (Miller, 1992). Cultures were incubated at 25°C or 37°C over night or until the culture reached an OD_{600} of approx. 0.6 - 0.8 (normally after 4 h of growth). 1 ml of exponentially grown cells and 500 µl of stationary cultures were spun down. The β- galactosidase activity was either directly determined or the pellets were stored at -20°C.
The pellets were resuspended in 200 µl Z-buffer (100 mM Na_2HPO_4 pH 7.0, 10 mM KCl, 1 mM $MgSO_4$) and diluted 1/10 in the same buffer for OD_{600} determination. Subsequently, 200 µl of this dilution were lysed using 10 µl 0.1 % SDS and 10 µl chloroform followed by 10 min incubation at room temperature. 1.8 ml Z-buffer was added and the reaction was started by the addition of 0.4 ml ONPG (4 mg/ml in H_2O). After appropriate coloration of the mixture the reaction was stopped by the addition of 1 M Na_2CO_3 and the OD_{420} was determined. The enzyme activity was calculated as shown below:

$$\text{specific activity } [\mu mol \cdot (mg \cdot min)^{-1}] = OD_{420} \times 6.75\ [\mu mol/min/mg] \times (OD_{600} \cdot \Delta t\ [min] \cdot V\ [l])^{-1}$$

OD_{420}:	optical density of stopped reaction
6.75:	extinction coefficient of cleaved ONPG
OD_{600}:	optical density of bacterial culture
V:	culture volume
Δt:	time from start to stop of enzyme reaction

2.2.4.2 SDS PAGE

SDS PAGE electrophoresis was carried out as described by Laemmli (Laemmli, 1970) in a vertical electrophoresis chamber (Mini Protean II, BioRad, München). Dependent on the protein size 12-15 % polyacrylamide separating gels with a 4 % stacking gel were used. Ingredients of an exemplary 15 % SDS gel are shown below (Table 7). Size separation was performed at 25 mA per gel at maximum voltage. As size standard the PageRuler™ prestained protein marker was used (Ferments, St. Leon-Rot) (Figure 20).

Table 7: Components used for a 15 % polyacrylamide gel.

Buffer	Amount
15 % separating gel	
separating gel buffer pH 8.8 (1.5 M Tris-HCl pH 8.8, 4 % SDS)	2.5 ml
acrylamide (30 %)	4 ml
H_2O *bidest*	2.5 ml
TEMED	50 µl
APS (10 %)	50 µl
4 % stacking gel	
stacking gel buffer (0.5 M Tris-HCl pH 6.8, 4 % SDS)	2.5 ml
acrylamide (30 %)	1.1 ml
H_2O *bidest*	6.5 ml
TEMED	40 µl
APS (10 %)	80 µl

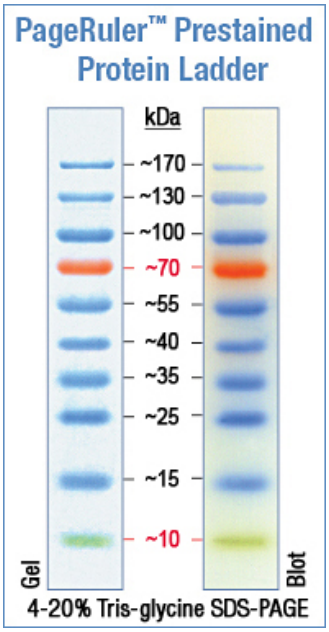


Figure 20: The PageRuler™ prestained protein marker was used as size standard for all protein polyacrylamide gels (Fermentas St. Leon-Rot).

For sample preparation, an OD_{600} equivalent of 1 was spun down and the pellet was resuspended in SDS sample buffer (60 mM Tris-HCl pH 6.8, 2 % SDS, 10 % glycerol, 3 % β-mercaptoethanol, 0.005 % bromophenol blue, H_2O) followed by a subsequent heat denaturation at 95°C for 10 min. If necessary (for whole cell extract) the samples were treated with benzonase (Fermentas, St. Leon Rot) for 10 min at RT. Subsequently, the gels were prepared for western blotting.

2.2.4.3 Western blot analysis

To specifically detect proteins western blot was performed. Proteins separated by SDS PAGE were transferred onto a nitrocellulose membrane (Millipore, Billerica) by wet blotting in a Mini-Protean II Western blot cell (BioRad, München). The membrane was first activated in methanol and the protein transfer was carried out in transblot buffer (25 mM Tris, 192 mM glycerol, 20 % methanol (v/v)) at 100 V for 1 h. Subsequently, the membrane was incubated in 3 % BSA in PBST (137 mM NaCl, 2.7 mM KCl, 45 mM Na_2HPO_4, 15 mM KH_2PO_4, 0.005 % Tween-20) over night to reduce unspecific antibody binding. After washing the membrane four times in PBST for 10 min each incubation with the primary antibody diluted in 3 % BSA

in PBST was carried out for 1 h followed by additional washing four times in PBST for 10 min each (antibodies used in this study are listed in Table 8). The membrane was then incubated with the horseradish peroxidase- coupled secondary antibody (anti-rabbit) diluted in 3 % BSA in PBST. After another four washing steps in 3 % BSA in PBST for 10 min each, the blots were developed using the Western Lightning ECL II Kit (Perkin Elmer, Waltham). Detection was carried out using the Chemi Doc XR System (BioRad, München).

Table 8: Antibodies used in this study.

Antibody	Manufacturer/Source	Dilution
Primary antibody		
Anti-Hfq	Davids Biotechnology, Regensburg	1:10000
Secondary antibody		
Anti-rabbit immunoglobulin horse radish peroxidase	NEB, Ipswich	1:10000

2.2.4.4 Electromobility shift assay (EMSA)

To analyze the binding capability of purified Crp protein to different promoter fragments, DNA electromobility shift assays were carried out. The Crp protein was purified as described previously (Heroven *et al.*, 2012). The DNA fragment of interest was mixed with fragments serving as negative control in equimolar amounts in 1 x Binding buffer (10 mM Tris-HCl pH 7.5, 1 mM EDTA, 5 mM DTT, 5 % glycerol, 10 mM NaCl, 1 mM $MgCl_2$, 0.1 mg/ml BSA). Increasing concentrations of Crp protein were added and the mixture was incubated at 30°C for 20 min. Subsequently, 15 µl were loaded on a 4 % native polyacrylamide gel (Table 9). Electrophoresis was performed at 70 V for 1 h and stained with ethidium bromide. Primers used for fragment amplification are indicated in Table 3.

Table 9: Composition of a 4 % native TBE polyacrylamide gel

Buffer	Amount
4 % TBE gel	
10 x TBE	0.5 ml
acrylamide (40 %)	5 ml
H_2O *bidest*	8,2 ml
rhinohide gel strengthener (Invitrogen, Carlsbad)	240 µl
TEMED	16 µl
APS (10 %)	66 µl

2.2.5 Bioinformatic methods

To search for DNA sequences of *Y. pseudotuberculosis* the online database Yersy (www.yersy.tu-bs.de) and Prodoric (http://prodoric.tu-bs.de) were used. Sequence alignments and sequence analysis of plasmids after sequencing were carried out using the program ApE (http://biologylabs.utah.edu/jorgensen/wayned/ape). ApE was furthermore used to generate vector maps.

The illustration of sequencing data obtained by 454 sequencing (Heroven, unpublished) and Illumina sequencing (Nuss, unpublished) was performed using the Artemis genome browser (http://www.sanger.ac.uk/resources/software/artemis).

To search for complementary sequences of the *Y. pseudotuberculosis* strain YPIII to the *Y. pseudotuberculosis* strain IP32953 and other species, the online search tool Blast (http://blast.ncbi.nlm.nih.gov/Blast.cgi) was used. Comparison to described RNA families was carried out using the RFAM online tool (http://rfam.sanger.ac.uk/).

Quantification of western blot signals was carried out using the software image J (http://rsbweb.nih.gov/ij/download.html).

2.2.6 Mouse infection

Animal work was performed in strict accordance with the German regulations of the Society for Laboratory Animal Science (GV-SOLAS) and the European Health Law of the Federation of

Laboratory Animal Science Associations (FELASA). The protocol was approved by the „Niedersächsisches Landesamt für Verbraucherschutz und Lebensmittelsicherheit: animal licensing committee permission no. 33.9-42502-04-12/0907“.

In order to assess the impact of sRNAs on *Y. pseudotuberculosis* virulence, groups of 7-week-old female BALB/c mice were orally infected with $1x10^8$ bacteria using a gavage needle. To prepare the inocula, the *Y. pseudotuberculosis* wild type strain IP32953 and isogenic mutant strains were cultivated overnight in LB medium at 25°C. The bacteria were harvested by centrifugation in a Sigma 3-18 K centrifuge using the 19776-H rotor for 10 min at 8,000 rpm, washed in sterile 1 x PBS and centrifuged a second time for 10 min at 8,000 rpm. The cells were resuspended in 1 x PBS (137 mM NaCl, 2.7 mM KCl, 45 mM Na_2HPO_4, 15 mM KH_2PO_4) and the cell density was adjusted according to the OD_{600}. To control the bacterial concentration, serial dilutions of the inocula were plated on LB agar plates. Four days post infection the bacterial load (colony forming units (CFU)/gram tissue) was determined in the Peyer´s patches, mesenterial lymph nodes, liver and spleen. Isolated Peyer´s patches were rinsed with sterile 1 x PBS and incubated with 100 µg/ml gentamicin in 1 x PBS for 30 min in order to kill bacteria on the luminal surface. Subsequently, three washing steps in 1 x PBS were performed to remove the gentamycin. All organs were weighed, homogenized in 1 x PBS, and two independent serial dilutions were plated on LB agar plates. Serial dilutions of the Peyer’s patches were plated on *Yersinia* selective agar (Oxoid, Basingstoke). The CFUs were counted to assess the bacterial load per gram tissue. For survival assays, groups (n=5) of 7-week-old BALB/c mice were orally infected with a dose of $1x10^8$ bacteria of *Y. pseudotuberculosis* wild type strain IP32953 and isogenic mutant strains (YPIP09, YPIP1). The body weight of the mice was monitored for 11 days.

3 Results

3.1 Identification of novel sRNAs in *Y. pseudotuberculosis* YPIII

3.1.1 Detection of sRNAs by 454 pyrosequencing

In the past, the impact of *Y. pseudotuberculosis* virulence factors and the mechanisms applied by this bacterium to maintain an infection were intensively studied. In nearly all studies only protein virulence factors were analyzed. A recent study dealt with the identification of novel sRNAs in *Y. pseudotuberculosis* IP32953. Furthermore, they characterized the impact of some sRNAs on *Yersinia* virulence and it became clear that sRNAs also play a crucial role during infection (Koo *et al.*, 2011). The study reported here aimed the identification of novel sRNAs in *Y. pseudotuberculosis* YPIII. RNA was isolated from wild type cultures grown at 25°C in the stationary growth phase and 37°C in exponential growth as well as from an *hfq* deletion strain (YP80) grown at 25°C to stationary phase. Previous studies showed that under *in vitro* conditions, growth at 25°C to the stationary phase induces expression of virulence genes necessary for the initial infection phase, e.g. *invA* or *rovA*. In contrast *in vitro* growth at 37°C to the exponential phase induces expression of virulence genes of the ongoing infection e.g. *yadA* or the *yop* genes. The *hfq* deficient strain was selected since the stability of many already known sRNAs mostly relies on this protein and different read counts would already hint to an Hfq dependency of these sRNAs. For RNA isolation the SV Total RNA Isolation Kit (Promega, Mannheim) and the miRNeasy Mini Kit (Qiagen, Hilden) for small sized RNA enrichment were used. Subsequently, the samples were first treated with Terminator Phosphate Dependent Exonuclease (TEX) to remove processed transcripts and second with tobacco acid pyrophosphatase (TAP) to remove the triphosphate for better linker ligation (Heroven, unpublished). Size fractionation for fragments between 50 and 500 nts was carried out at GATC Biotech (Konstanz) and 454 sequencing was performed using the Genome Sequencer GS FLX (Roche, Mannheim). A sequencing depth of 839,786 reads was reached. In total 52,165 reads mapped uniquely to the *Y. pseudotuberculosis* YPIII chromosome and the virulence plasmid pYV.

The sequencing results were analyzed bioinformatically (Reinkensmeier, University of Bielefeld). A fist bioinformatic attempted defined an sRNA to have a size of 50-500 nts and a permanent coverage of 5 reads minimum. That identified 320 putative novel sRNA out of which 20 were encoded on the *Yersinia* virulence plasmid pYV (Appendix Table S 1-4). First trails to validate some of theses sRNAs failed. Therefore, the bioinformatic criteria were changed. The coverage of the previously identified sRNAs was examined and only candidates with a minimum coverage of 10 reads at at least one position were taken into account.
By that, a number of 169 putative novel sRNAs were identified (seven on the virulence plasmid pYV). The sRNAs were classified as described in the introduction (Figure 1) and 52 *trans*-encoded sRNAs, 26 *cis*-encoded antisense sRNAs, and 91 mRNA leader structures were found (Figure 21). Details on the sRNAs and their expression profile are indicated in Table S 1-4. Out of the 52 *trans*-encoded sRNAs 17 were described in *E. coli* or *Salmonella* (ca. 10 %). Furthermore, about 50 % of all detected sRNAs showed a different read count in the *hfq* deletion strain compared to the wild type indicating an Hfq dependency of these transcripts.

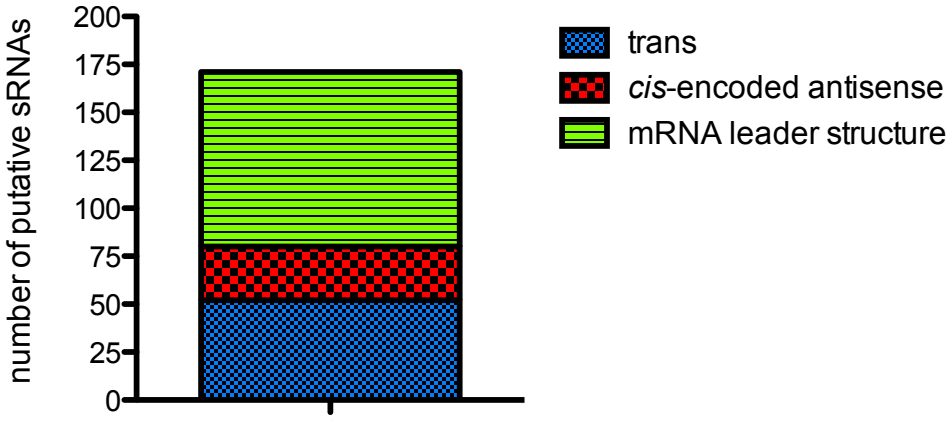


Figure 21: Relative proportion of sRNA candidates of the different classes identified by 454 sequencing. Number of sRNAs identified when the bioinformatic parameters defined a seed region to have a coverage of at least 10 reads. For size determination the seed region was extended at both ends until the coverage dropped below 5 reads.

Furthermore, the conservation of these transcripts was examined. Therefore, a BLAST search was used and availability of the sRNA sequence in other species was analyzed. An sRNA was considered to be conserved, when a sequence coverage of 50 % with a sequence conservation of more than 90% was present. The highest amount of sRNAs was conserved within *Y. pseudotuberculosis* and *Y. pestis* (54 %). The second largest group encompassed

sRNAs that were conserved within the γ-proteobacteria (25 %). In addition, a relatively high number of sRNAs was only conserved within the pathogenic *Yersinia* species (15 %) while a few sRNAs could only be detected in *Y. pseudotuberculosis* wild type strain YPIII (4 %) or in different *Y. pseudotuberculosis* isolates e.g. IP32953, IP2666 (2 %) (Figure 22).

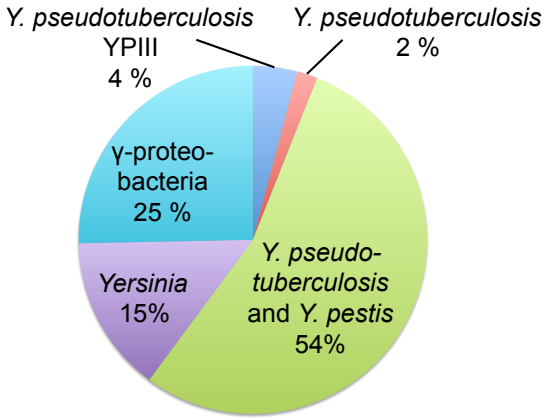


Figure 22: Diagram indicating the conservation of the sRNAs identified by 454 sequencing.

3.1.2 Verification of identified small *trans*-encoded sRNAs

In order to experimentally verify the *trans*-encoded sRNAs and their expression profile identified by 454 sequencing (Table S 1), northern hybridization was carried out for twelve *trans*-encoded sRNAs with homologies to sRNAs of other *Enterobacteriaceae* and twelve newly described candidates. Total RNA was isolated from both the wild type strain and the *hfq* deletion strain grown at 25°C or 37°C in exponential and stationary growth using the SV total RNA isolation Kit (Promega, Mannheim).

Northern blot analysis of sRNAs with homologies to sRNAs of other *Enterobacteriaceae*

The detection of sRNAs by 454 sequencing was performed using RNA from the wild type grown at 25°C to the stationary growth and at 37°C in the exponential growth phase. In addition, the expression was analyzed in a Δ*hfq* mutant grown at 25°C to stationary growth.

The *Y. pseudotuberculosis* sRNAs with homologies to the previously described sRNAs SraH, Spot42, RybB, RyhB, GlmY, CyaR, GcvB, RyeB, OmrA/B, MicM GlmZ and FnrS of *E. coli* and *Salmonella* were all detectable by northern blotting (Figure 23). These sRNAs were shown to

be involved in pathways contributing to the iron metabolism, cell wall synthesis, regulation of outer membrane protein production, or catabolite repression (Massé and Gottesman, 2002; Møller *et al.*, 2002; Kalamorz *et al.*, 2007; Papenfort *et al.*, 2008; Reichenbach *et al.*, 2008).

The 454 data indicated an Hfq dependency at 25°C in stationary growth for all of theses sRNAs except GcvB. In most cases less sRNA was detected by northern blotting in the *hfq* deletion strain but in the case of Spot42 more RNA was detected. Even though the 454 sequencing data indicated no *hfq* dependency for GcvB northern blotting detected elevated sRNA levels in a Δ*hfq* mutant at 25°C in the stationary growth phase. Equal RyeB levels were detected by northern blotting in both strains even though the 454 pyrosequencing indicated a downregulation. Further, the either positive or negative effect of Hfq on an sRNA was also observed in the other growth conditions.

Additionally, the expression pattern indicated by 454 sequencing at 25°C in the stationary growth phase compared to 37°C in exponential growth was consisted with the northern blot analysis for Spot 42, RyhB, GlmY, CyaR, GlmZ, FnrS, and RybB. The expression of SraH, RyeB, MicM, OmrA/B and GcvB did not reflect the expression pattern detected by 454 sequencing.

In general, all of the analyzed candidates showed differential expression either in response to temperature or growth phase.

Taken together, the detection of all sRNAs was possible but the expression pattern indicated by 454 sequencing did not always meet the sRNA levels detected by northern blotting. The expression of most sRNAs was induced in stationary growth and dependent on Hfq.

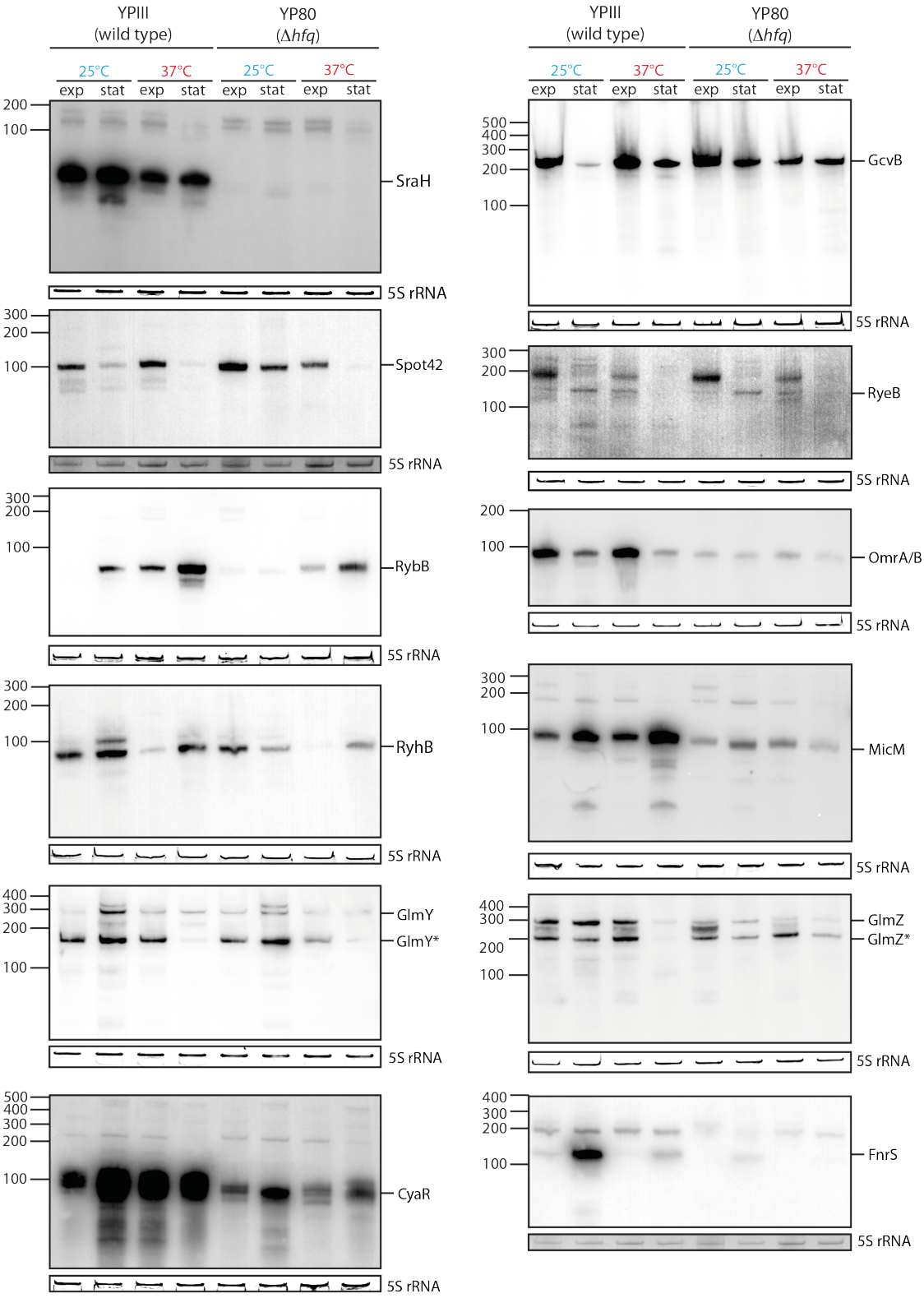


Figure 23: Northern blot analysis of selected sRNAs with homologies to previously described sRNAs. Bacteria were grown at the indicated conditions and the total RNA was isolated using the SV total RNA Isolation Kit (Promega, Mannheim). 10 µg total RNA were separated on a 7 M urea/12 % acrylamide gel. Specific oligomer probes were labeled with γ-ATP^{32}. Detection was carried out using the Typhoon FLA-9000 (GE healthcare, Chalfont St Giles). The * indicates processed variants of the sRNAs. Northern blots were carried out in duplicates. 5S rRNA served as loading control, the size standard is indicated on the left in nts.

Analysis of the transcription of selected sRNAs with homologies to other *Enterobacteriaceae*

In order to further investigate the environmental regulation observed in the northern blotting experiments, the transcription of selected sRNA candidates was analyzed by β-galactosidase activity assays. Approx. 500 nts upstream of the transcriptional start site (TSS) predicted by the 454 sequencing data were cloned in front of the promoter-less *lacZ* gene. The resulting plasmids were transformed in either the *Y. pseudotuberculosis* wild type stain YPIII or the isogenic Δ*hfq* mutant YP80. The bacteria were grown at 25°C and 37°C to exponential or stationary growth and the β-galactosidase activity was analyzed. Figure 24 illustrates the transcription rate from the MicM, FnrS, RyhB, and Spot42 promoter region.

Even though clear bands were detected by northern blotting the activity of both the *micM* and the r*yhB* reporter constructs was similar to the basal level of the empty vector control (Figure 23, Figure 24 B and C). The expression of the *lacZ* reporter from the potential *fnrS* promoter slightly exceeded the basal level at 25°C in stationary growth and 37°C in exponential growth. The highest promoter activity was detected at 37°C in the stationary growth phase (Figure 24 A). This stands in contrast to the northern blot analysis where the strongest expression was observed at 25°C in stationary growth (Figure 23). These data hint to a strong posttranscriptional regulation of the sRNA expression indicating a low transcription level with a long half-life of the transcript.

In the wild type the putative GlmY, GlmZ, and RybB sRNA reporter constructs were also only weakly expressed after growth at 25°C or 37°C in the exponential or stationary growth phase (Figure S 1).

Only the expression from the *spot42* promoter region reflects the expression pattern detected by northern blotting (Figure 23, Figure 24 D). In both wild type and the Δ*hfq* mutant strain the highest transcription was measured in the exponential growth phase similar to the sRNA levels observed by northern blotting. In addition, only weak reporter activity and low sRNA amounts of Spot42 were detectable in the stationary growth phase. The elevated Spot42 levels in the Δ*hfq* mutant strain grown at 25°C were confirmed by a higher β-galactosidase activity. However, at 37°C in the Δ*hfq* mutant no elevated levels of Spot42 could be detected by northern blotting even though a higher reporter activity was measured. This might indicate a posttranscriptional regulation that counteracts the effect of a Δ*hfq* deletion at 37°C.

Taken together, these data indicate that the transcription of an sRNA might not automatically reflect the sRNA levels in the cell. Further, in nearly all cases the enzymatic activity was very low indicating a low transcription rate. This suggests that these sRNAs might be very stable and only a low transcription rate is necessary to maintain the intracellular sRNA levels.

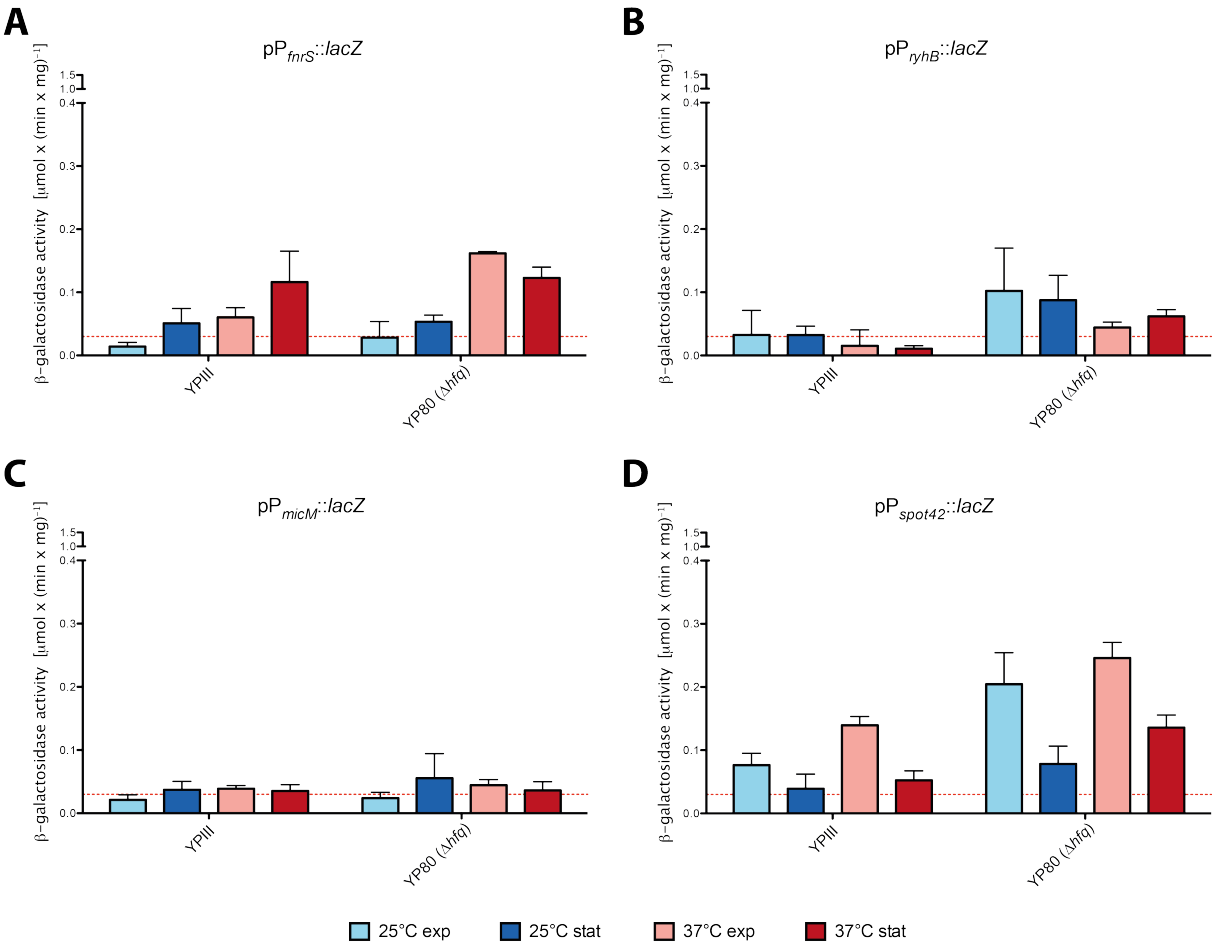


Figure 24: Expression of the *fnrS*-, *ryhB*-, *micM*-, and *spot42-lacZ* reporter constructs in response to temperature and growth phase. Strains YPIII and YP80 (Δ*hfq)* harboring the respective *lacZ* reporter construct were grown in LB medium at 25°C or 37°C to either exponential or stationary growth. After harvesting, the cells were lysed and the β-galactosidase activity was determined and is given in [µmol x (min x mg) $^{-1}$]. The red line indicates the basal activity of the empty vector control**.** The data represent the average and the standard deviation from at least three independent experiments each done in duplicates.

Northern blot analysis of putative novel sRNAs

In addition to the twelve sRNAs with homologies to sRNAs of other *Enterobacteriaceae*, twelve newly identified sRNAs were selected for verification by northern blotting (Figure 25). At the time when the experiments started these sRNAs did not show any homology to

already described sRNAs. Two of these sRNAs (YpseC0109, YpseC0279) were described quite recently in both *Y. pestis* and *Y. pseudotuberculosis* (Ysr100, Ysr164) (Beauregard *et al.*, 2013). The *Y. pseudotuberculosis* wild type strain YPIII and the isogenic Δ*hfq* mutant strains YP80 were incubated at both 25°C and 37°C in LB medium to exponential or stationary growth and total RNA was isolated.

The presence of all selected candidates could be validated. The 454 data indicated a downregulation in the Δ*hfq* mutant compared to the wild type grown at 25°C in the stationary growth phase for the sRNAs YpseC0098, YpseC0109, YpseC0125, and YpseC0209, respectively, which was confirmed for the latter three. As indicated from the 454 data analysis the remaining eight sRNAs were equally synthesized in both strains.

The 454 data indicated a temperature and/or growth phase dependent regulation for all selected candidates comparing the sRNA levels from 25°C in stationary growth to 37°C in exponential growth. A growth phase and/or temperature dependency was detectable in all cases. The expression changes of YpseC0170, YpseC0201, YpseC0179, and YpseC0285 did not reflect the 454 sequencing data (for comparison see Table S 1).

In general, these results indicate, that the newly identified sRNAs exist in *Y. pseudotuberculosis* YPIII and their expression is dependent on the growth phase, temperature, and the presents of the Hfq protein.

Further, ten of the twelve sRNAs showed a multiple band pattern after northern blotting. Two fragments of the sRNA YpseC0201 were detected by northern blotting. A smaller sized fragment was only detectable in the exponential growth phase and a bigger sized fragment in the stationary growth phase. The size predicted by 454 sequencing represents the smaller sized fragment. This indicates that the sRNAs might be transcribed as longer primary transcripts and subsequently becomes processed.

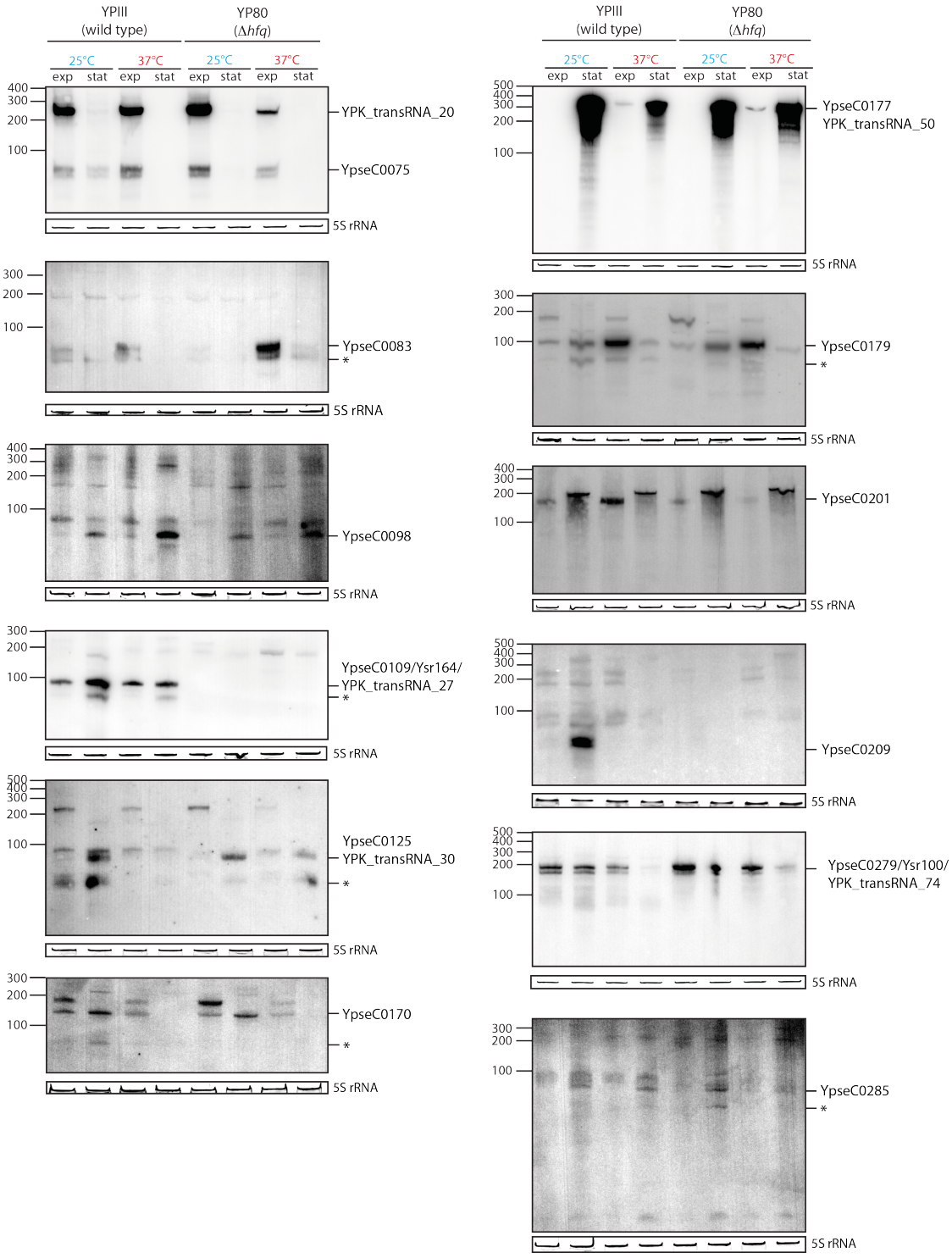


Figure 25: Northern blot analysis of newly identified *trans*-encoded sRNAs. Bacteria were grown at the indicated conditions and the total RNA was isolated using the SV total RNA Isolation Kit (Promega, Mannheim). 10 µg total RNA were separated on a 7 M urea/12 % acrylamide gel. Specific oligomer probes were labeled with γ-ATP^{32}. Detection was carried out using the Typhoon FLA-9000 (GE healthcare, Chalfont St Giles). The * indicates putative processed variants of the sRNAs. Northern blots were carried out in duplicates. The indicated names of the sRNAs correspond to the designated names of the 454 sequencing and the RNA-Seq as well as the names published previously (see section 3.2) (Koo *et al.*, 2011; Beauregard *et al.*, 2013). 5S rRNA served as loading control, the size standard is indicated on the left in nts.

Analysis of the transcription of selected putative sRNAs

The influence of temperature and growth phase on the expression of newly identified sRNAs was further characterized by *lacZ* reporter assays. As described previously, 500 nts upstream of the TSS predicted by 454 sequencing were cloned in front of the *lacZ* gene. The resulting plasmid was transformed into the wild type strain YPIII and the isogenic Δ*hfq* deletion strain. YpseC0083 and YpseC0201 were chosen, since both sRNAs are not or only partially conserved in different *Y. pseudotuberculosis* strains while YpseC0125 is conserved among *Y. pseudotuberculosis* and *Y. pesits* and YpseC0170 in γ-proteobacteria. The bacteria were grown at 25°C and 37°C to both the exponential and stationary growth phase and the *lacZ* reporter expression is summarized in Figure 26.

YpseC0201 was clearly detectable by northern blotting (Figure 25) but the activity of the corresponding reporter construct did not exceed the activity of the empty vector control (Figure 26 D).

Expression of the YpseC0083 reporter construct increased during stationary growth. This stands in contrast to the northern blotting analysis, where the highest sRNA levels were detectable at 37°C in the exponential growth phase (Figure 25). In contrast, in a Δ*hfq* deletion strain the expression of the YpseC0083 reporter construct was induced at 37°C compared to the wild type (Figure 26 A). Since this regulation was detectable by both northern blotting and reporter analysis, this indicates that elevated transcription of the sRNA is responsible for the higher sRNAs levels.

The β-galactosidase activity of the YpseC0125-*lacZ* reporter construct in bacteria grown at 25°C was higher in the stationary growth phase, similar to the RNA levels detected by northern blotting (Figure 25, Figure 26 B). The strongest β-galactosidase expression was observed at 37°C during the stationary growth. In this condition no transcript could be detected by northern blotting, indicating that a posttranscriptional effect might lead to a degradation of the sRNA.

The highest expression was found for the YpseC0170-*lacZ* construct (Figure 26 C). Consistent with the northern blot analysis, stronger induction of the expression of the *lacZ* reporter was detected at 25°C compared to 37°C (Figure 25, Figure 26 C).

Similar to the experiments carried out with the *fnrS, ryhB, micM* and *spot42* reporter constructs, these data indicate 1. that the transcription of the identified sRNAs in general is

low, 2. that the transcription is often dependent on temperature and growth phase, and 3. that the transcription of the sRNA does not directly indicate the intracellular sRNA levels.

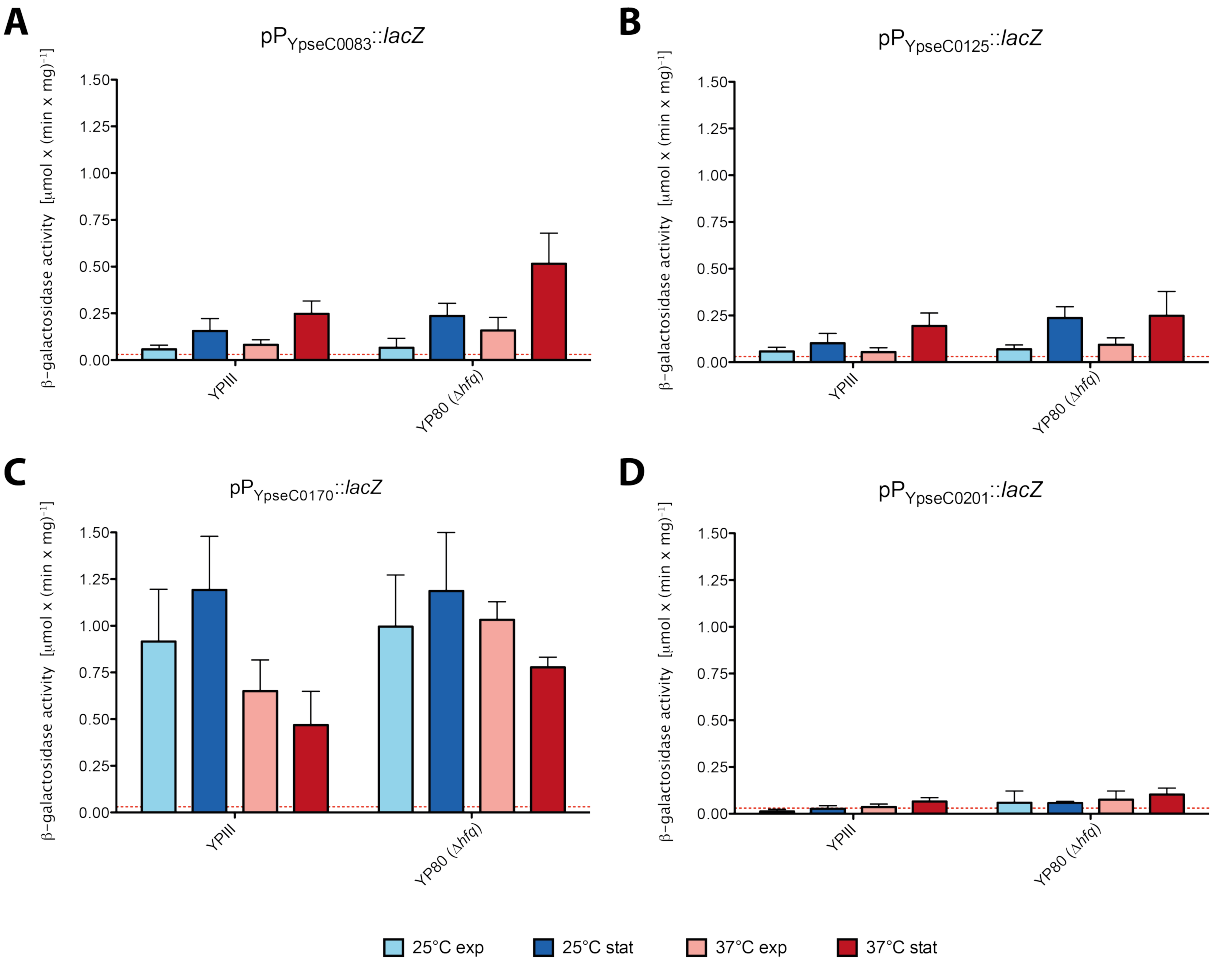


Figure 26: Expression of YpseC0083-, YpseC0125, YpseC0170, and YpseC0201-*lacZ* reporter constructs in response to temperature and growth phase. Strains YPIII and YP80 (Δ*hfq)* harboring the respective *lacZ* reporter construct were grown in LB medium at 25°C or 37°C to either exponential or stationary growth. After harvesting, the cells were lysed and the β-galactosidase activity was determined and is given in [µmol x (min x mg)$^{-1}$]. The red line indicates the basal activity of the empty vector control**.** The data represent the average and the standard deviation from at least three independent experiments each done in duplicates.

3.1.3 Verification of identified small *cis*-encoded antisense sRNAs by northern blotting

In addition to *trans*-encoded sRNAs, *cis*-encoded antisense sRNAs were detected by 454 sequencing. Therefore, the expression of theses sRNAs was also validated using northern blotting to verify the 454 sequencing data. Northern blot analysis was carried out for nine candidates using total RNA isolated form the wild type strain YPIII and the isogenic Δ*hfq*

deletion strain grown in LB medium at 25°C or 37°C to the exponential or stationary growth phase. Hybridization using specific probes for the selected sRNAs gave signals in at least one of these conditions (Figure 27). Four out of the nine sRNAs showed additional shorter fragments, which might indicate processing of the sRNAs. Additionally, longer fragments of four sRNAs were detectable, which hints to the existence of primary transcripts.

The size estimated after 454 sequencing (Appendix Table S 2) could be verified for all sRNAs except YpseC0230. In this case a size of 86 nts was predicted but the northern blot analysis revealed a size of about 180 nts. This might be explained by a lower coverage of the flanking regions of the sRNA. In summary this indicates, that the size predicted from the 454 sequencing might reflect processed fragments of the sRNAs. However, binding of the probe to unspecific RNA fragments cannot be excluded.

YpseC0081, YpseC0190, and YpseC0293 were indicated by 454 sequencing to be Hfq dependent at 25°C in the stationary growth phase. The northern blot analysis confirmed this for YpseC0081 and YpseC0190 but YpseC0293 showed steady state levels in both the wild type and the Δ*hfq* mutant strain. Consistent with the 454 sequencing data the remaining candidates showed no Hfq dependency.

The 454 sequencing data indicated a temperature and/or growth phase dependent expression of all detected sRNAs. The predicted expression pattern was experimentally validated for YpseC0015, YpseC0054, YpseC0055, YpseC0081, YpseC0162, YpseC0190, and YpseC0293. The detected sRNA levels of YpseC0036 and YpseC0230 were not consistent with the 454 sequencing data.

These results furthermore confirm the 454 sequencing data. In addition to the existence of the *cis*-encoded antisense sRNAs the expression profile was confirmed. However, the size detected by 454 sequencing may not be reliable, since these samples were enriched for small sized fragments.

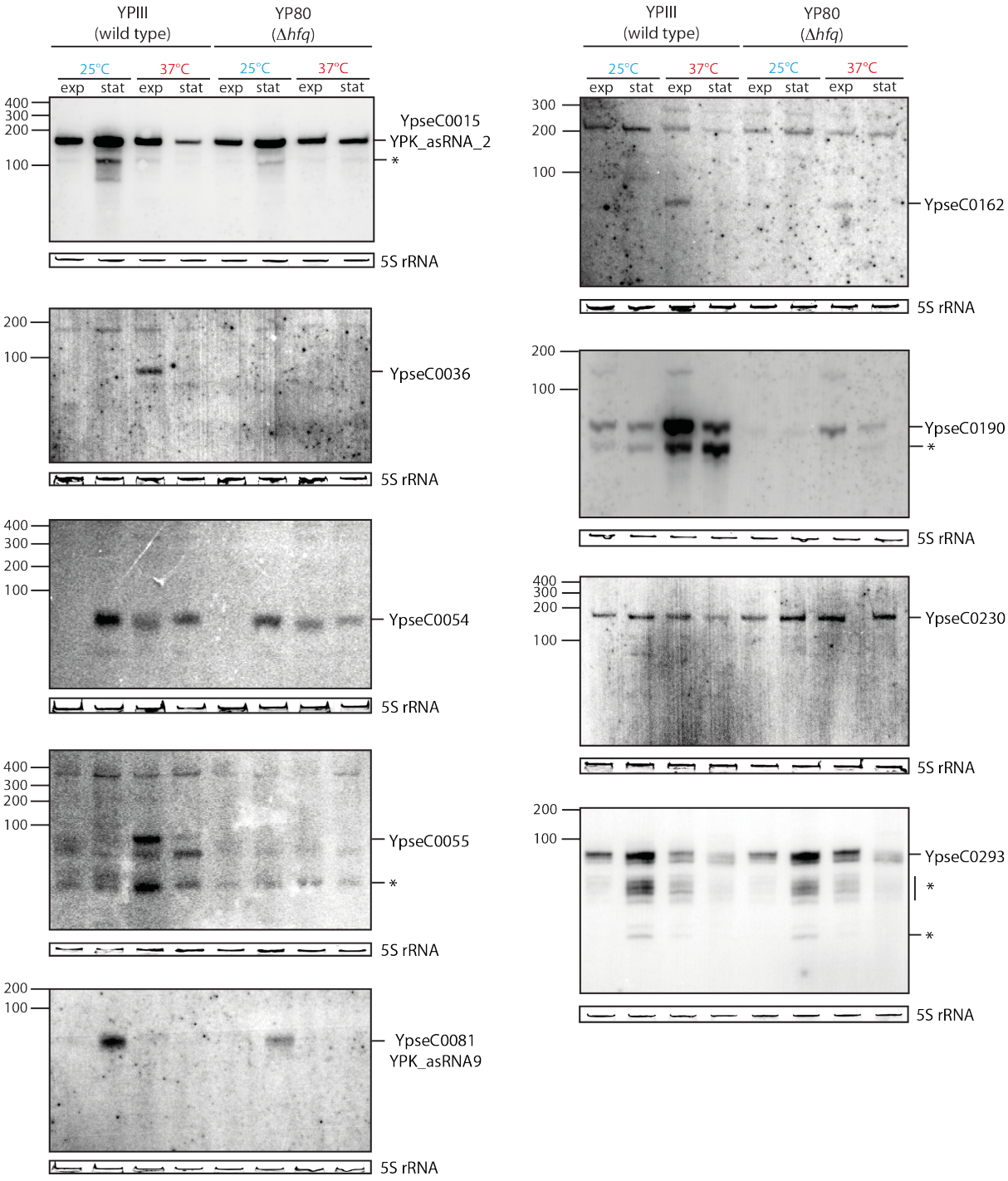


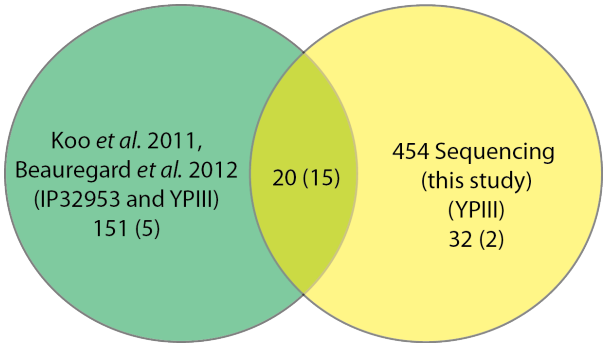
Figure 27: Northern blot analysis of newly identified *cis*-encoded antisense sRNAs. Bacteria were grown at the indicated conditions and the total RNA was isolated using the SV total RNA Isolation Kit (Promega, Mannheim). 10 µg total RNA were separated on a 7 M urea/12 % acrylamide gel. Specific oligomer probes were labeled with γ-ATP^{32}. Detection was carried out using the Typhoon FLA-9000 (GE healthcare, Chalfont St Giles). The * indicates putative processed variants of the sRNAs. Northern blots were carried out in duplicates. The indicated names of the sRNAs correspond to the designated names of the 454 sequencing and the RNA-Seq (see section 3.2). The 5S rRNA served as loading control, the size standard is indicated on the left in nts.

3.1.4 Strain- and method-dependent detection of sRNAs in *Y. pseudotuberculosis*

During the course of this study two other studies were published which reported the identification of novel sRNAs in the *Y. pseudotuberculosis* clinical isolate IP32953 as well as in *Y. pestis* Kim6+ (Koo *et al.*, 2011; Beauregard *et al.*, 2013). These studies aimed only the identification of *trans*-encoded sRNAs.

A comparison of the *trans*-encoded sRNAs identified by 454 sequencing and the sRNAs identified by Beauregard *et al*., 2013, and Koo *et al*., 2011 revealed that approx. 50 % of the sRNAs identified by 454 sequencing were also detected in these studies (20 sRNAs; Figure 28 A). In general, about 70 % of these overlapping *trans* sRNAs showed homologies to already described sRNAs e.g. GlmY, GlmZ, MicM, RyhB, OmrA/B (Figure 28 B). Most recent, two studies identified sRNAs in the highly mouse virulent *Y. pestis* strain 201 and the human-avirulence strain 91001 (Qu *et al.*, 2012; Yan *et al.*, 2013). Only sRNAs with homologies to sRNAs of other *Enterobacteriaceae* were found in their studies and the 454 sequencing reported here (e.g. CyaR, OmrA/B, 6S RNA, RyhB).

A



B

Conserved in	Number	Name
Y. pseudotuberculosis	1	YpseC0182/Ysr114
Y. pseudotuberculosis and *Y. pestis*	6	MicM, CyaR, YpseC0279/Ysr100, YpseC0109/Ysr 164, YpseC0108/Ysr20, YpseC0189/Ysr62
Yersinia	2	GlmZ, OmrA/B
γ-proteobacteria	11	RyeB, SsrA, SRP_bact, Fnrs, GlmY, CsrB, 6S , GcvB, MicA, RyhB, Spot42

Figure 28: Overlap of *trans*-encoded sRNAs identified by 454 sequencing and in previous studies (Koo *et al.*, 2011; Beauregard *et al.*, 2013). (A) Venn diagram illustrating the overlap of sRNAs comparing the *trans*-encoded sRNAs of *Y. pseudotuberculosis* identified in this study and by Koo *et al.,* 2011 and Beauregard *et al.,* 2012. The number of sRNAs with homologies to other *Enterobacteriaceae* is shown in brackets. (B) Table illustrating the conservation of the overlapping sRNAs. The indicated names were either given by the study reported here or by Koo *et al.,* 2011.

The relatively low overlap between the *trans*-encoded sRNAs may be explained by several reasons. The major differences between the work presented here and the data published by Koo *et al*., 2011 were the strains (YPIII vs. IP32953), different growth conditions (LB medium vs. BHI medium) and different detection methods (454 sequencing vs. Illumina sequencing). Furthermore, different bioinformatic setups were used, which might explain the high variation of the identified sRNAs.

In order to analyze which of these reasons might explain the small overlap, the detection of five sRNAs identified by Koo *et al*., 2011 but not in the 454 sequencing was carried out using the *Y. pseudotuberculosis* IP32953 and YPIII isolate after growth in LB and BHI medium. Total RNA was isolated from both wild type strains grown either in BHI or LB medium at 25°C or 37°C to the exponential or stationary growth phase, while the respective Δ*hfq* mutant was grown at 25°C to stationary growth.

The sRNA Ysr12 was detectable in both strains grown in LB and BHI medium (Figure 29 A). *Y. pseudotuberculosis* YPIII grown in LB medium expressed the sRNA at 25°C in the exponential growth phase and in the stationary growth phase, one of the conditions used for 454 sequencing. This indicates, that a method/sequencing-dependent detection of sRNAs might exist. When the bacteria were grown in BHI medium a detection was only possible at 25°C during stationary growth. Further, only a slight Hfq dependency was detectable in LB medium, while a stronger dependency was observed in BHI medium. The expression of Ysr12 in the *Y. pseudotuberculosis* IP32953 strain showed a growth phase dependency but no temperature dependency. Further, only a slight medium dependent expression was detectable.

Ysr10 was detectable in both the YPIII and IP32953 clinical isolate grown in BHI medium but a detection of this sRNA in LB medium failed (Figure 29 B). The expression profile was similar in both strains with the small difference that a processed form of Ysr10 was detectable in *Y. pseudotuberculosis* IP32953 while this processing does either not happen in the YPIII strain or the processed transcript is quickly degraded and therefore not detectable by northern blotting.

The sRNA Ysr18 was only detected in *Y. pseudotuberculosis* IP32953. Neither in LB nor in BHI medium *Y. pseudotuberculosis* YPIII expressed this sRNA (Figure 29 C). The remaining two sRNAs Ysr17 and Ysr19 were only detected in the IP32953 strain grown in BHI medium (Figure 29 D). Koo *et al.,* 2011 reported the expression to be induced in the stationary growth phase, but the sRNAs were only detected in the exponential growth phase. This might be explained by differences in the BHI medium. While Koo *et al.,* 2011 used sterile filtered BHI medium, the medium used in the study reported here was autoclaved, which might destroy some nutrients.

These data indicate a strain- as well as growth medium-dependent expression of the sRNAs. These results further suggest that some of the sRNAs might not have been detected due to method/sequencing specific limitation.

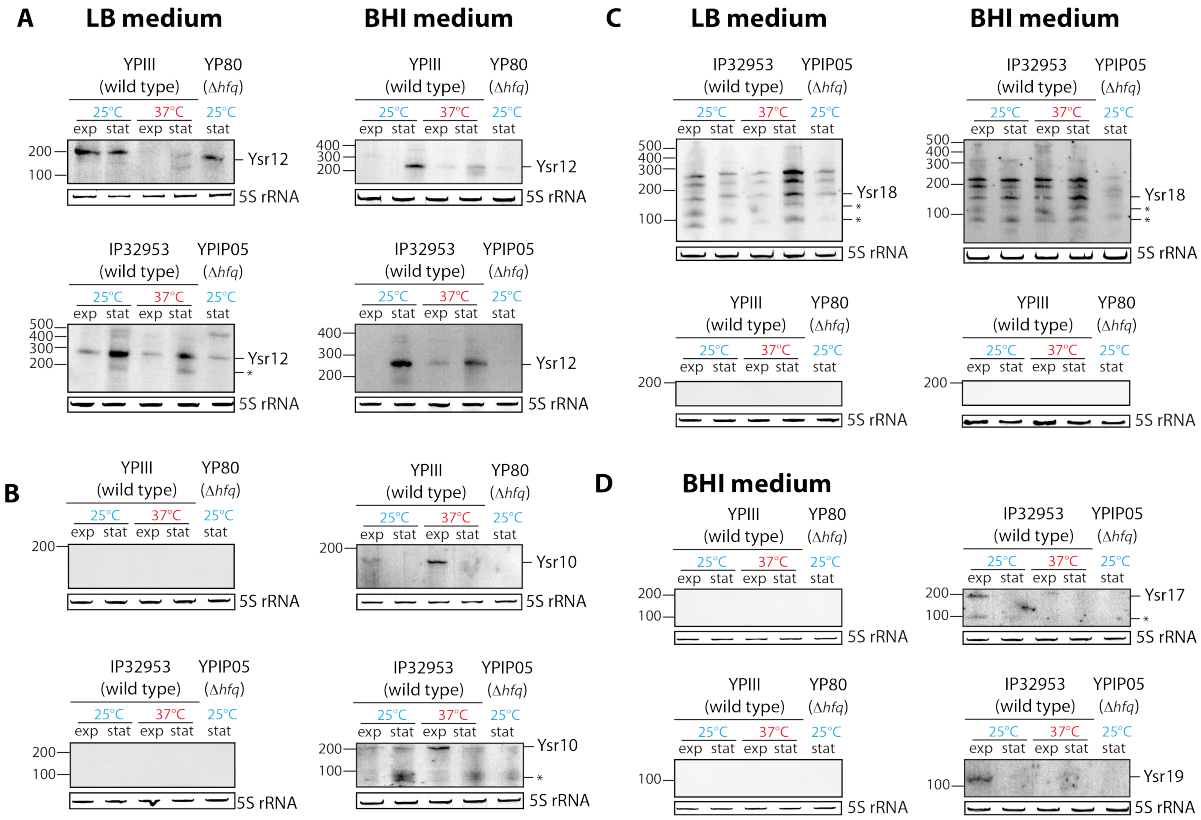


Figure 29: Detection of sRNAs by northern blotting after growth of the *Y. pseudotuberculosis* wild type strains IP32953 and YPIII and their isogenic *hfq* deletion strains in LB or BHI medium. Bacteria were grown at the indicated conditions and the total RNA was isolated using the SV total RNA Isolation Kit (Promega, Mannheim). 10 µg total RNA were separated on a 7 M urea/12 % acrylamide gel and northern blots were carried out in duplicates. Specific oligomer probes were labeled with γ-ATP^{32}. The * indicates putative processed variants of the sRNAs. The sRNA names rely on the names given by Koo *et al.* 2011. The 5S rRNA served as loading control, the size standard is indicated on the left in nts. (A) Detection of the sRNA Ysr12 in both strains in both media. (B) Detection of the sRNAs Ysr10 in both strains but only in LB medium. (C) Detection of Ysr18 was only possible in the IP32953 strain in both media but not in the YPIII strain. (D) Ysr17 and Ysr19 were only detected in BHI medium in the IP32953 strain.

3.2 Transcriptomic profiling of *Y. pseudotuberculosis* YPIII

In the course of this study an in-house facility for Illumina sequencing became available. One advantage of Illumina sequencing in comparison to 454 pyrosequencing are deeper sequencing results, which allow the identification of additional sRNAs. Further, the transcriptomic landscape of a bacterium can be analyzed with respect to differential gene expression and the determination of transcriptional start sites. Therefore, a high-throughput sequencing was carried out to identify additional sRNAs and the transcriptome of *Y. pseudotuberculosis* YPIII (Nuss, unpublished). Temperature strongly influences the expression of virulence associated genes e.g. *invA* and *yadA*. Furthermore, growth phase is an important environmental signal for *Yersinia* to differentially regulate virulence gene expression (e.g. *rovA* and *cnfY*). Therefore, the transcriptomic profile of sRNA from bacteria grown at 25°C or 37°C to the exponential or stationary growth phase was determined. In addition to temperature and growth phase the nutrient availability strongly influences gene expression in bacteria. The Crp protein is one of the most important global regulators of *Y. pseudotuberculosis* that links metabolism to virulence (Heroven *et al.*, 2012). The sRNAs Spot42 and CyaR are the only sRNAs that were reported to be regulated by Crp but a global approach searching for further candidates was not performed (Papenfort *et al.*, 2008; Beisel and Storz, 2011). Additionally, the role of Crp on gene expression was so far only determined at 25°C. Therefore, this study intended the identification of further Crp regulated sRNA and the analysis of the composition of genes of the Crp regulon at 25°C and 37°C after stationary growth.

Total RNA was isolated using the hot phenol method to avoid sample biasing by a column-based method. After rRNA depletion the samples were split and three out of four pooled samples were treated with TAP while one remained untreated. TAP removes the 5’ triphosphate of primary transcripts, which is necessary for 5’ linker adaptation. Therefore, samples treated with TAP were enriched in primary transcripts, while samples without TAP treatment contained mostly processed transcripts. Subsequently, strand-specific cDNA libraries were synthesized and multiplex samples were sequenced using the HiSeq2000 and the Genome Analyzer IIx Illumina systems. Each library (16 in total) was sequenced with 2-14 mio reads. Jan Reinkensmeier, University of Bielefeld, then mapped the reads to the *Y. pseudotuberculosis* YPIII genome and the virulence plasmid pYV using Bowtie2 (Version 2.1.0) and carried out the following bioinformatic analysis (Langmead and Salzberg, 2012).

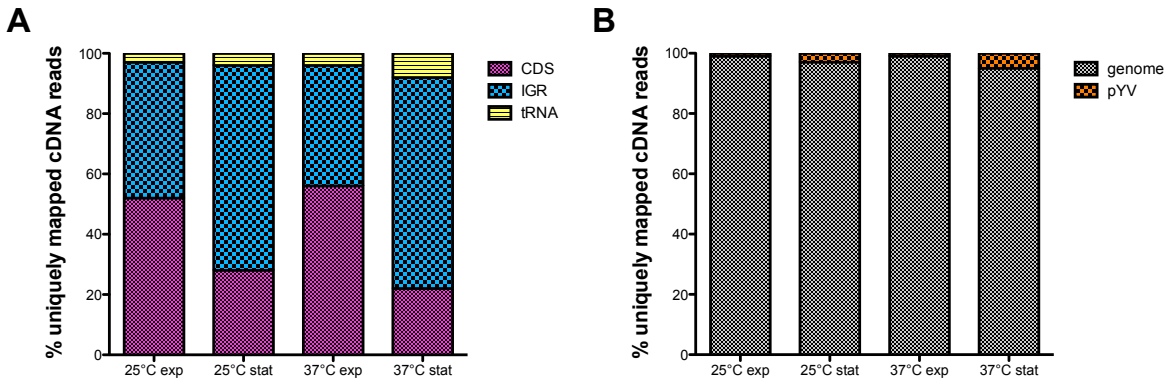


Figure 30: Percentage of uniquely mapped reads determined from TAP treated samples. (A) Number of reads mapped to coding sequences (CDS) and intergenic regions (IGS) as well as tRNA sequences. (B) Percentage of uniquely mapped reads that mapped either to the genome or the virulence plasmid pYV.

In exponential growth 50 % of the unique reads mapped to coding sequences, while the remaining 50 % mapped to intergenic regions. Interestingly, in the stationary growth phase approx. 70 % of all uniquely mapped reads covered intergenic regions (Figure 30 A). This indicates that an upregulation of sRNA expression might take place. In addition, more reads were mapped to the virulence plasmid pYV at 37°C (5 %) (Figure 30 B), which is in agreement with the finding that virulence associated genes of the ongoing infection such as *yadA* are upregulated at 37°C (Skurnik and Toivanen, 1992).

3.2.1 Identification of noncoding RNAs (sRNAs) by Illumina sequencing

In order to identify novel sRNAs, the Illumina sequencing data were analyzed using the following bioinformatic criteria. An sRNA was defined to carry a seed region with a length of 40 nts and a continuous coverage of at least 30 reads in one condition. For size determination the seed region was extended until the coverage dropped below 1/10 reads of the maximum coverage. Thereby, a number of 163 putative non-coding sRNAs were identified, out of which 83 were classified as *trans*-encoded sRNAs, and 80 candidates as *cis*-encoded antisense sRNAs (Appendix Table S 5, 6). Out of these putative *trans*-encoded sRNAs, 81 were encoded on the chromosome while only two were located on the virulence plasmid pYV. 57 out of the 80 *cis*-encoded antisense sRNAs were encoded on the

chromosome. Conspicuously, 18 antisense sRNAs were located on the virulence plasmid. Not all detected sRNAs were found in the wild type strain. Out of the 83 *trans*-encoded sRNAs six could only be detected in the Δ*crp* mutant strain, while three antisense sRNAs were only detected after sequencing of the Δ*crp* strain (Appendix Table S 5, 6).

Furthermore, the conservation of all detected sRNAs was analyzed by BLAST search. An sRNA was considered to be conserved, when a sequence coverage of 50 % with a sequence conservation of more than 90% was present. The most abundant group of sRNAs was conserved in *Y. pseudotuberculosis* and *Y. pestis* (81 in total). The second and third biggest groups are conserved within the genus *Yersinia* (39 in total) and in the γ-proteobacteria (25 in total). Four sRNAs were only found in *Y. pseudotuberculosis* species e.g. YPIII, IP32953, IP2666, while 14 sRNAs were only present in the *Y. pseudotuberculosis* wild type strain YPIII (for details see Appendix Table S 5, 6, Figure 31).

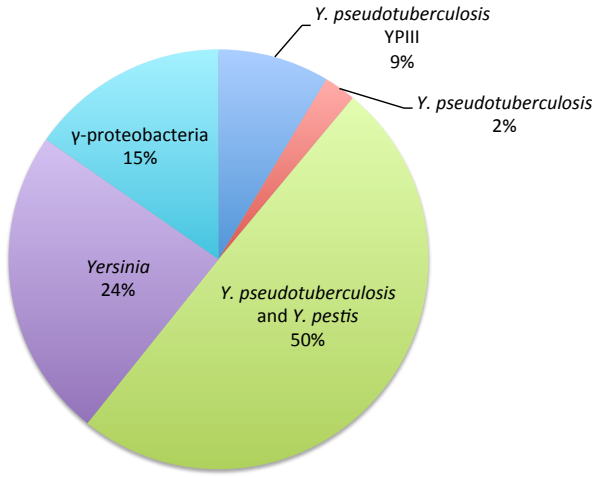


Figure 31: Diagram indicating the conservation of the sRNAs identified by Illumina sequencing.

3.2.1.1 Temperature- and growth phase-dependent expression of sRNAs

Comparative RNA-Seq was performed using the DESeq package to quantify and compare global sRNA levels with special emphasis on temperature- and growth phase-regulation. The sRNA expression at 25°C during exponential growth was compared to the expression in the stationary phase. Additionally, the expression at 25°C in the exponential growth phase was compared to the expression at 37°C in exponential growth.

An sRNA was considered to be differentially regulated, if a fold change ≥ 2 with a p-value ≤0.05 was present. Additionally, in at least one condition a coverage above 30 reads needed to be present. In total, a 70 sRNAs were differentially expressed whereby 52 sRNAs were dependent on the growth phase, 9 were temperature-dependent and 9 were dependent on both temperature and growth phase.

In order to validate the newly reported sRNAs, northern blot analysis was carried out. In *E. coli* and *Salmonella* many sRNAs have been reported to be Hfq dependent. This was also shown for several sRNAs detected by 454 sequencing. Therefore, the impact of Hfq on sRNAs identified by Illumina sequencing was also examined. Total RNA of the wild type and the isogenic Δ*hfq* mutant grown at 25°C and 37°C to exponential and stationary growth was isolated. Five *trans*-encoded and ten *cis*-encoded antisense sRNAs were selected for northern blotting (Figure 32). While the detection of all *trans*-encoded sRNA candidates was possible, the detection of two *cis*-encoded antisense sRNAs failed.

In total, six candidate sRNAs showed an Hfq dependent expression pattern (YPK_transRNA_37, YPK_transRNA_48, YPK_transRNA_58, YPK_asRNA_23, YPK_asRNA_24, YPK_asRNA_46). YPK_transRNA_58 showed higher sRNA levels in the Δ*hfq* strain, while the remaining five candidates were less abundant in the Δ*hfq* mutant strain.

The growth phase-dependent expression profile indicated by the Illumina data of six candidates could be validated (for details see Appendix Table S 5, 6). The Illumina sequencing did not predicted a growth phase dependency for seven candidates but they were either more or less abundant in stationary growth.

The temperature-dependency indicated by Illumina sequencing (for details see Appendix Table S 5, 6) of nine candidates was confirmed. The expression profile of YPK_asRNA_1 and YPK_asRNA_50 was not validated. YPK_transRNA_58 was not indicated to be temperature regulated but an upregulation was detectable by northern blotting. Interestingly, the Illumina data did not predict a temperature dependency of YPK_transRNA_58, since the read counts were slightly below the threshold. A lower threshold would also indicate this sRNA to be temperature-dependent.

YPK_asRNA_59 showed a strong growth phase-dependency and a slight temperature-dependent expression even though no dependency on these conditions was indicated by Illumina sequencing.

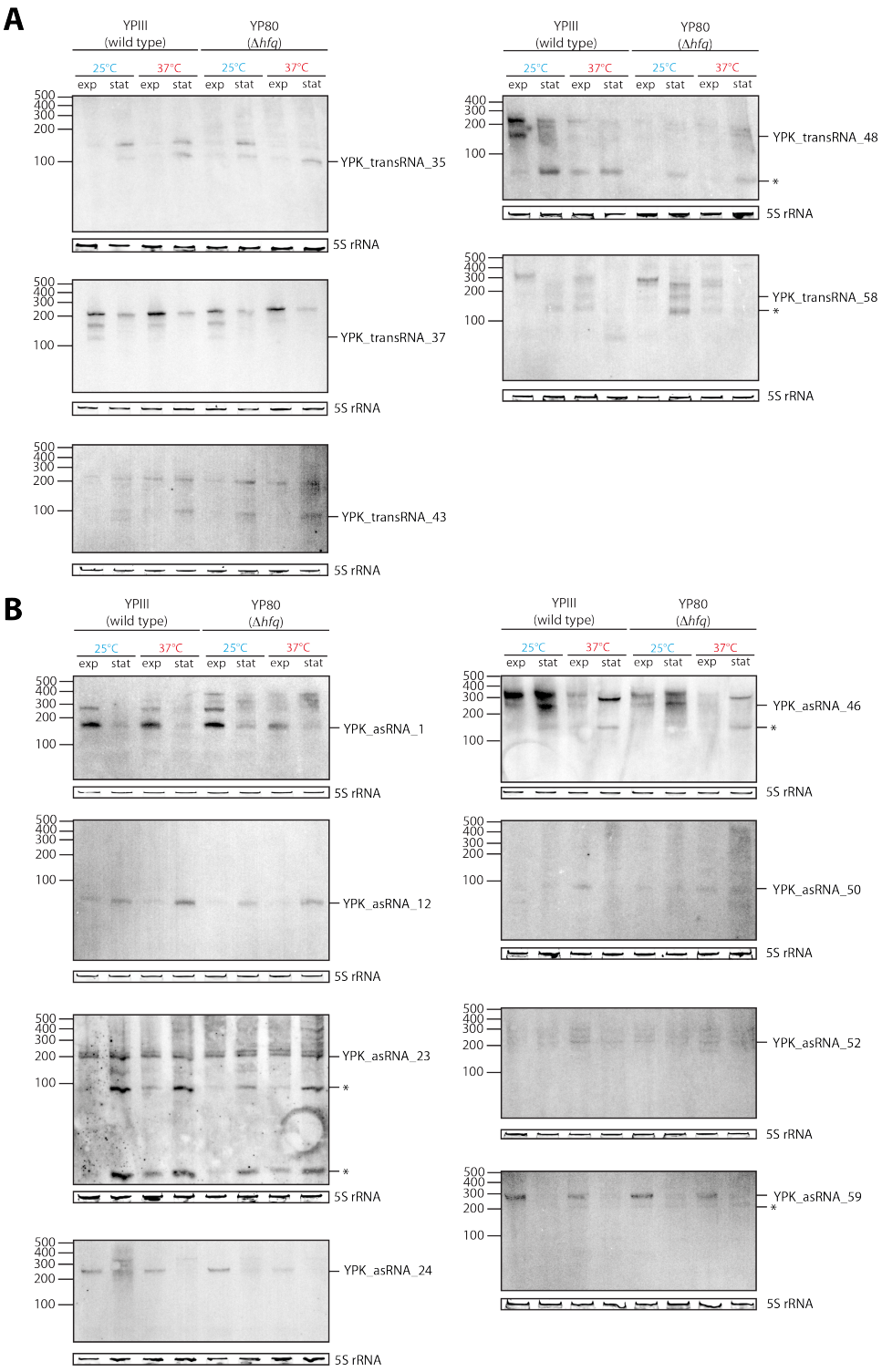


Figure 32: Northern blot analysis of newly identified sRNAs. Bacteria were grown at the indicated conditions and the total RNA was isolated using the SV total RNA Isolation Kit (Promega, Mannheim). 10 µg total RNA were separated on a 7 M urea/12 % acrylamide gel. Specific oligomer probes were labeled with γ-ATP[32]. The * indicates putative processed variants of the sRNAs. Northern blotting was carried out in duplicates. The indicated names of the sRNAs correspond to the designated names of the RNA-Seq. The 5S rRNA served as loading control, the size standard is on the left indicated in nts. (A) Detection of *trans*-encodes sRNAs. (B) Detection of *cis*-encoded antisense sRNAs.

sRNAs identified by 454 sequencing were also used for the validation of the Illumina sequencing data. Out of the 33 sRNAs validating the 454 sequencing data (see Figure 23, Figure 25, Figure 27) 16 were also detected by the Illumina sequencing approach (see Appendix Table S 1, 2, 5, 6). The results summarizing the comparison between the Illumina sequencing data and the northern blot analysis are listed in Table 10.

The growth phase-dependent expression was confirmed for 10 of these sRNAs. The northern blot analysis detected steady state levels after growth at 25°C in the exponential and stationary growth phase of one sRNAs even though the Illumina sequencing predicted differential expression (YPK_transRNA_74; Figure 23, 25). Additional five candidates were predicted to show steady state levels but a growth phase-dependent expression was detected by northern blotting (YPK_asRNA_9, Spot42, MicM, OmrA/B, RybB; Figure 23).

The temperature-dependent expression of 11 candidate sRNAs was confirmed. Two other candidates showed a temperature-dependency, which was not predicted from the RNA-Seq data (CyaR, MicM). The RNA-Seq data predicted a temperature-dependent upregulation of GlmY, but steady state levels were detected by northern blotting. In contrast to the Illumina data, YPK_transRNA_20 and YPK_transRNA_27 were more abundant at 37°C in the northern blot analysis, instead of less abundant.

Table 10: Temperature- and growth phase-dependent expression changes of sRNAs. Illustrated is the expression change from exponential to stationary growth and from 25°C to 37°C. Upregulation is illustrated by ↑, downregulation by ↓. No significant expression changes are illustrated by –. Green indicates overlap between Illumina sequencing and northern blotting, while red indicates no coincidence.

Name sRNA	Growth phase dependency		Temperature dependency	
	Illumina sequencing	Northern blotting	Illumina sequencing	Northern blotting
YPK_asRNA_1	-	↓	↑	-
YPK_asRNA_2	↑	↑	-	-
YPK_asRNA_9	-	↑	-	-
YPK_asRNA_12	↑	↑	-	-
YPK_asRNA_23	↑	↑	-	-
YPK_asRNA_24	-	↓	-	-

Name sRNA	Growth phase dependency		Temperature dependency	
YPK_asRNA_46	-	↑	↓	↓
YPK_asRNA_50	-	-	-	↑
YPK_asRNA_52	-	-	↑	↑
YPK_asRNA_59	-	↓	-	↓
YPK_transRNA_20	↓	↓	↓	↑
YPK_transRNA_27	↑	↑	↓	↑
YPK_transRNA_30	-	↑	-	-
YPK_transRNA_35	↑	↑	-	-
YPK_transRNA_37	-	↓	↓	↓
YPK_transRNA_43	-	↑	-	-
YPK_transRNA_48	-	↓	↓	↓
YPK_transRNA_50	↑	↑	-	-
YPK_transRNA_58	↑	↑	-	↑
YPK_transRNA_74	↑	-	-	-
SraH	↑	↑	-	↓
GcvB	↓	↓	-	-
RybB	↑	↑	↑	↑
GlmY	↑	↑	↓	-
CyaR	↑	↑	-	↑
GlmZ	↑	↑	-	-
Spot42	-	↓	-	-
MicM	-	↑	-	↑
OmrA/B	-	↓	-	-
RyhB	-	↑	↓	↓

In summary, the northern blot experiments confirm the existence of the selected sRNAs. Approx. 40 % of the sRNAs showed an Hfq-dependency. Additionally, the temperature-and growth phase-dependent expression was confirmed in most cases. Interestingly, those candidates were no growth phase-dependent expression was indicated by Illumina sequencing showed a growth phase-dependent sRNA expression (13 candidates). This might be due to the stringent bioinformatic criteria. To be defined as differentially regulated a fold

change ≥ 2 needed to be present with a p-value ≤ 0.05. Additionally, a coverage above 30 reads needed to be present in at least one condition. In all cases only one of these requirements was not fulfilled but the tendency in the Illumina sequencing was consistent with the expression pattern detected by northern blotting. This indicates, that even less stringent bioinformatic criteria allow to predict the correct sRNA expression.

18 *cis*-encoded antisense sRNAs were detected on the virulence plasmid pYV. The verification of these sRNAs was difficult, which might be due to a low abundance of these sRNAs. Only one candidate was detected by northern blotting and its expression pattern was confirmed experimentally (Figure 33).

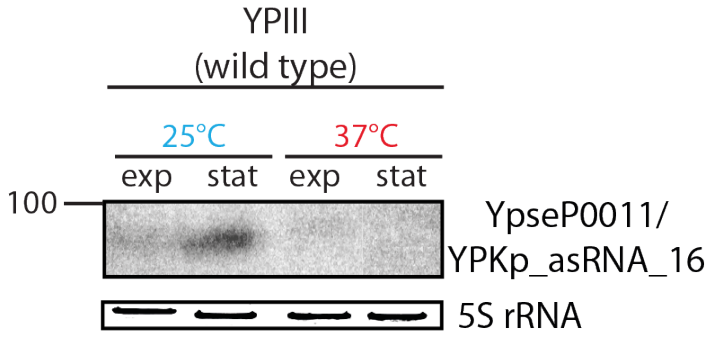
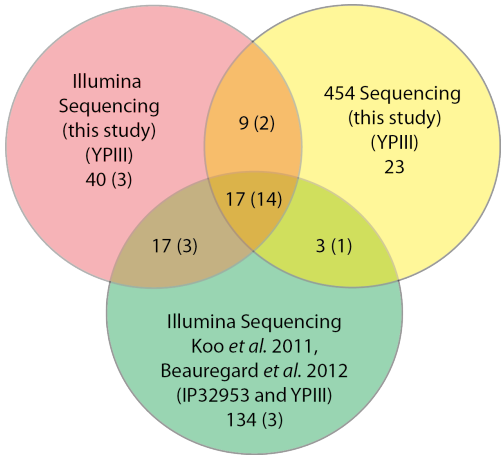


Figure 33: Detection of one virulence plasmid pYV encoded sRNAs. Bacteria were grown at the indicated conditions and the total RNA was isolated using the SV total RNA Isolation Kit (Promega, Mannheim). 20 µg total RNA were separated on a 7 M urea/12 % acrylamide gel. Specific oligomer probes were labeled with γ-ATP^{32}. Northern blotting was carried out in duplicates. The indicated names of the sRNAs correspond to the designated names of the 454 sequencing and the RNA-Seq (see section 3.1). The 5S rRNA served as loading control, the size standard is indicated on the left in nts.

In addition, the *trans*-encoded sRNAs identified by the approach reported here were compared to the sRNAs identified by the 454 sequencing approach and the studies published by Koo *et al.,* 2011 and Beauregard *et al.* 2013 (Figure 34). Approx. half of the sRNAs identified by Illumina sequencing were also identified by these three analyses, while only 30 % overlapped between the Illumina sequencing and the 454 sequencing approach reported here. An even smaller overlap exists for antisense transcripts (approx. 10 %) comparing the sRNAs identified by Illumina sequencing and the 454 sequencing approach. The overlap to the most recently published sRNAs in *Y. pestis* was only one *trans*-encoded sRNA and one *cis*-encoded antisense sRNA (Qu *et al.*, 2012; Yan *et al.*, 2013).

A



B

Conserved in	Number	Name
Y. pseudotuberculosis and *Y. pestis*	5	YPK_transRNA_27/YpseC0109/Ysr164, YPK_transRNA_54/YpseC0189/Ysr62, YPK_transRNA_74/YpseC0279/Ysr100, CyaR, MicM
Yersinia	2	GlmZ, OmrA/B
γ-proteobacteria	10	SraC, SsrA, SRP_bact, GlmY, CsrB, 6S, Spot42, GcvB, MicA, RyhB

Figure 34: Overlap of *trans*-encoded sRNAs identified in previous studies, by Illumina sequencing, and 454 sequencing (Koo *et al.*, 2011; Beauregard *et al.*, 2013). (A) Venn diagram illustrating the overlap. The numbers in front of the brackets indicate the total number of sRNAs belonging to the indicated group. The Numbers in brackets indicate the amount of sRNAs with homologies to other *Enterobacteriaceae*. (B) Table indicating the conservation of the overlapping sRNAs. The indicated names were given by 454 sequencing, Illumina sequencing and by Koo et al. 2011.

3.2.1.2 Verification of Crp-dependent sRNA expression

Additionally, the Crp-dependent sRNA expression was analyzed by DESeq. Out of the 163 identified sRNAs 91 showed a Crp-dependent expression (Appendix Table S 5, 6). Interestingly, nine of these sRNAs could not be detected in the wild type strain but only in the Δ*crp* libraries (YPK_transRNA_10, YPK_transRNA_13, YPK_transRNA_30, YPK_transRNA_38, YPK_transRNA_62, YPK_transRNA_71, YPK_asRNA_9, YPK_asRNA_34, YPKp_asRNA_5).

In order to validate the Crp-dependency of twelve selected sRNAs northern blot experiments were carried out (Figure 35). Total RNA was isolated from the wild type strain and the

isogenic Δ*crp* mutant grown at 25°C and 37°C to the stationary growth phase. CyaR was already described to be Crp-dependent and was therefore used as positive control.

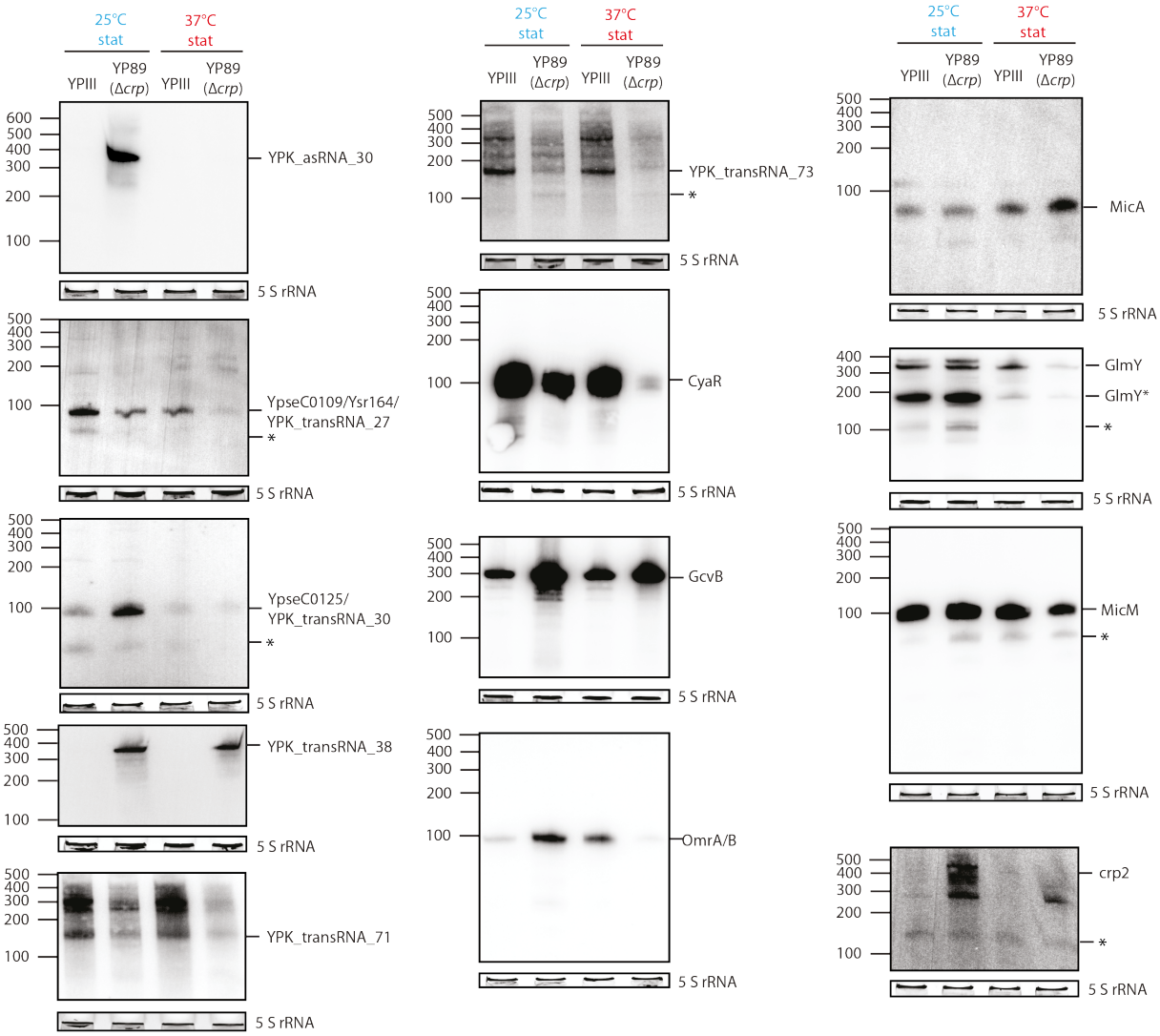


Figure 35: Detection of Crp-dependent sRNAs by northern blotting. Bacteria were grown at the indicated conditions and the total RNA was isolated using the SV total RNA Isolation Kit (Promega, Mannheim). 10 µg total RNA were separated on a 7 M urea/12 % acrylamide gel. Specific oligomer probes were labeled with γ-ATP[32]. Detection was carried out using the Typhoon FLA-9000 (GE healthcare, Chalfont St Giles). The * indicates putative processed variants of the sRNAs. Northern blotting was carried out in duplicates. The indicated names of the sRNAs correspond to the designated names of RNA-Seq. The 5S rRNA served as loading control, the size standard is indicated on the left in nts.

The Crp-dependent expression of six candidates was confirmed by northern blotting at both temperatures (YPK_asRNA_30, YPK_transRNA_38, YPK_transRNA_27, YPK_transRNA_30, CyaR, MicA), while the expression of three candidates was only confirmed at 25°C (GcvB, OmrA/B, GlmY) and the expression of one sRNA only at 37°C (YPK_transRNA_73). The

expression pattern of MicM and YPK_transRNA_71 predicted by Illumina sequencing could not be verified at 25°C and 37°C.

Surprisingly, in all cases higher sRNA levels were detectable in the *crp* deletion strain grown at 25°C. This might indicate, that the deletion of *crp* might lead to a completely different composition of the total RNA.

Interestingly, OmrA/B levels were counterregulated at 25°C and 37°C. At 25°C the deletion of *crp* resulted in higher sRNA levels, while less sRNA was detected in the *crp* deletion strain grown at 37°C. This indicates, that Crp regulated OmrA/B in a different manner at different temperatures.

In addition, manual data analysis of the Illumina data identified a putative sRNA (crp2) that harbors a perfect Crp-binding site in its upstream region. This sRNA was detected with less than 30 reads and is therefore not listed in Table S 5. Since the sRNA was only detectable after sequencing of the Δ*crp* libraries the influence of Crp on crp2 was also tested by northern blotting and the Crp dependency was confirmed. Although the sRNA could not be detected in the wild type strain a strong signal was detectable in a Δ*crp* mutant.

Taken together, these data indicate that not only CyaR and Spot42 are expressed in a Crp-dependent manner but Crp influenced the expression of several sRNAs.

3.2.2 Comparative analysis of the *Y. pseudotuberculosis* YPIII transcriptome

3.2.2.1 Influence of temperature and growth phase on the gene expression of *Y. pseudotuberculosis*

In order to investigate the temperature- and growth phase-dependent gene expression of *Y. pseudotuberculosis* on a global level, gene expression of all identified genes was compared during growth in the exponential and stationary growth phase and at 25°C and 37°C during the exponential growth phase. In total, the expression of 1585 genes was growth phase-dependent (Table S 7), while 824 genes were found to be temperature regulated (Table S 8). In both cases about 50 % of all genes were upregulated, while the other half was downregulated (growth phase-dependent downregulated: 799 genes, upregulated: 786 genes; temperature-dependent downregulated: 395 genes, upregulated: 429 genes).

Most of the genes that showed a differential expression profile in a growth phase dependent manner were associated with metabolism and information storage and processing. Especially, genes involved in energy production and conservation (3 % of all regulated genes), amino acid metabolism (6 % of all regulated genes) and translation (9 % of all regulated genes) were downregulated. The majority of upregulated genes were associated with amino acid and carbohydrate metabolism (6 % and 5 % of all regulated genes, respectively) (Figure 36 A).

Temperature mainly influences genes associated to metabolism and information storage and processing but also virulence associated genes. Many genes related to virulence were upregulated at 37°C (6 % of all regulated genes) as well as genes that associate with energy conservation (6 % of all regulated genes) and amino acid and carbohydrate transport and metabolism (8 %, respectively). The major group of downregulated genes included translation-associated genes (10 % of all regulated genes) (Figure 36 B).

In order to verify the observed temperature- and growth phase-dependent gene expression identified by high-throughput sequencing, qRT-PCR was performed. Growth phase-dependent expression of 17 selected candidates was verified (Figure 37 A). The tendency of their expression change could be confirmed for all candidates but in some cases the absolute fold change did not reflect the fold change indicated by Illumina sequencing.

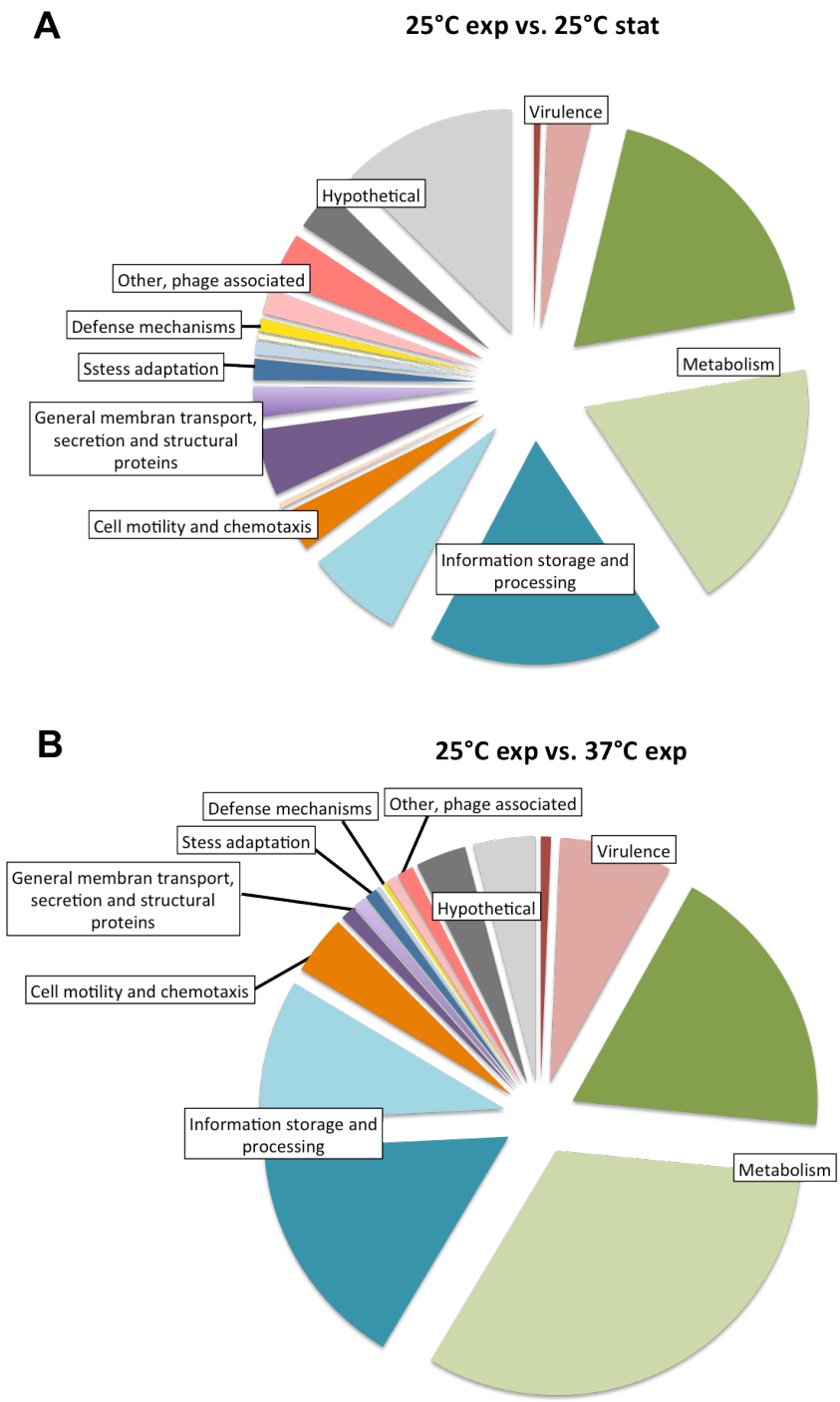


Figure 36: Pie chart illustrating the differentially regulated genes when the temperature- and growth phase- dependent gene expression was analyzed. (A) Comparison of gene expression at 25°C in exponential vs. stationary growth and (B) in exponential growth at 25°C vs. 37°C. Colors indicate different categories of gene function. Red: virulence-associated genes, green: metabolism-associated genes, turquoise: information storage and processing, orange: information storage and processing, orange: Cell motility and chemotaxis-associated, purple: general membrane transport, secretion and structural proteins, blue: stress adaptation, yellow: defense mechanisms, rosé: other, phase associated, grey: hypothetical proteins. Light colors indicate the number of upregulated genes while dark colors indicate downregulated genes.

Moreover, the temperature-dependent expression of 21 selected genes was analyzed comparing gene expression after exponential growth at 25°C vs. 37°C (Figure 37 B). In general, the expression change of all candidates was confirmed using qRT-PCR. The fold change detected by qRT-PCR of 17 candidates was consisted with the fold change calculated from the RNA-Seq data. However, qRT-PCR indicated higher fold changes of YPK_0152, YPK_2197, YPK_3388, and *fliA* than reported in the RNA-Seq data.

Taken together, the transcriptional landscape of *Y. pseudotuberculosis* is strongly dependent on temperature and growth phase. Additionally, the differential gene expression of selected candidates was verified and in most cases the fold change calculated after Illumina sequencing was proven.

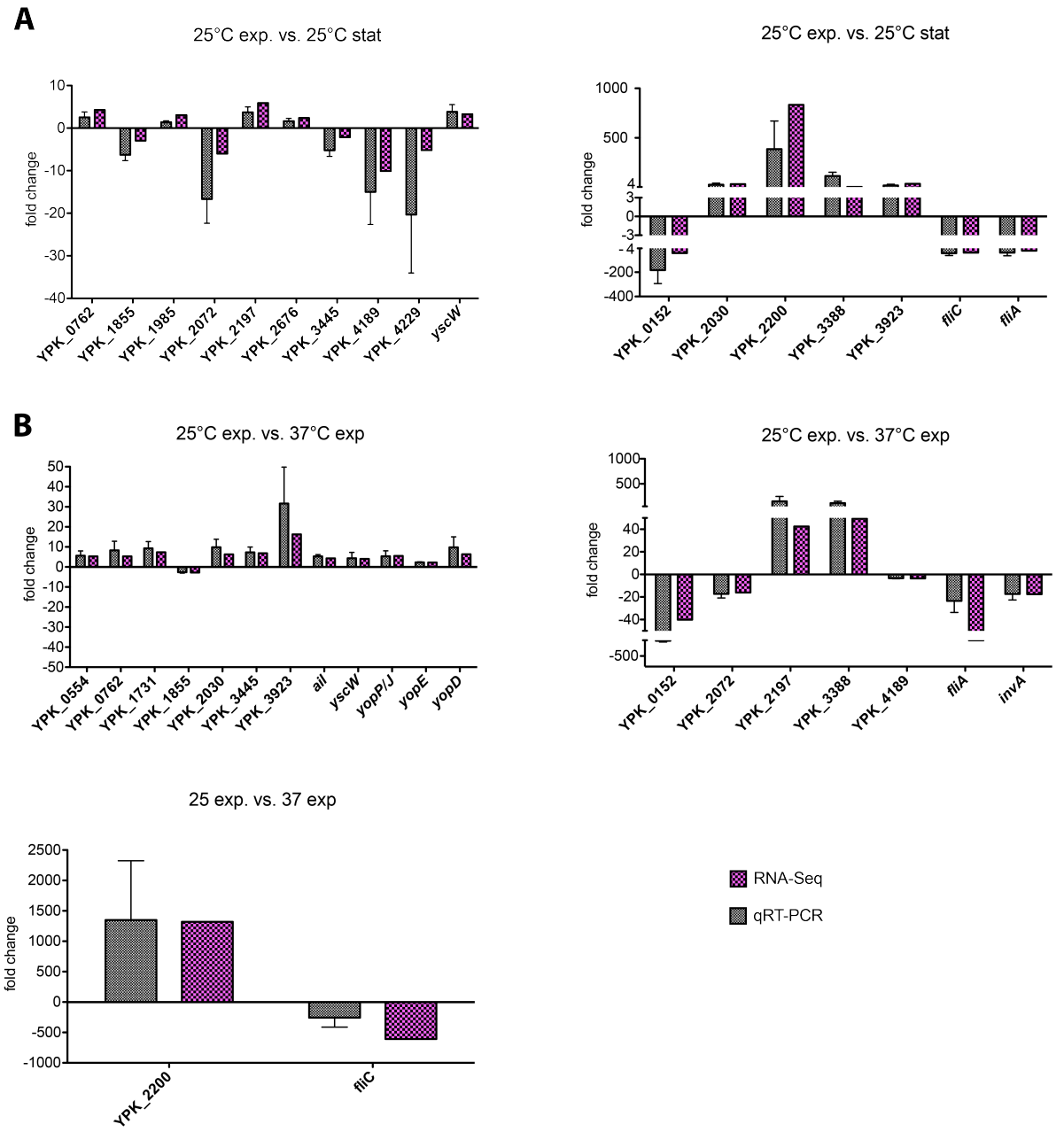


Figure 37: Validation of temperature- and growth phase-dependent gene expression identified by RNA-Seq using qRT-PCR. Purple bars indicate the fold change detected by RNA-Seq, grey bars indicate the fold change detected by qRT-PCR. The fold change after qRT-PCR was calculated as described previously in relation to the 5 S rRNA (Pfaffl, 2001). (A) Fold changes detected by qRT-PCR and RNA-Seq between exponential and stationary growth at 25°C. (B) Fold changes detected by qRT-PCR and RNA-Seq between exponential growth at 25°C and 37°C.

3.2.2.2 Crp-dependent gene expression in *Y. pseudotuberculosis* YPIII

In addition to the identification of the temperature and growth phase-dependent transcriptome the impact of Crp on gene expression was determined. Therefore, the *crp* deletion strain (YP89) was grown at 25°C or 37°C until the bacteria reached the stationary growth phase. Subsequently, total RNA was isolated and TAP treated samples were sequenced. Gene expression in the *crp* deletion strain was compared to the wild type strain grown under the same condition. Thereby, 963 genes were found to be differentially regulated out of which 563 were differentially regulated at 25°C (Table S 9) and 414 were differentially regulated at 37°C (Table S 10). Over all, 50 % of these genes were either up- or downregulated (25°C: 253 downregulated, 310 upregulated; 37°C: 180 downregulated, 234 upregulated). Approx. 80 % of the genes that were found to be downregulated at 37°C were also downregulated at 25°C, while about 35% of the upregulated genes at 37°C were also upregulated at 25°C.

Further, the differentially regulated genes in the Δ*crp* strain were compared to those genes in the wild type that were regulated by growth phase. Approx. 50 % of the genes that were upregulated in the Δ*crp* mutant grown at 25°C were downregulated when growth phase dependent gene expression was monitored in the wild type grown to stationary growth. Similar, 50 % of the downregulated genes in the Δ*crp* mutant were upregulated at 25°C in the stationary growth phase. This indicates, that Crp is a regulator controlling gene expression in a growth phase dependent manner.

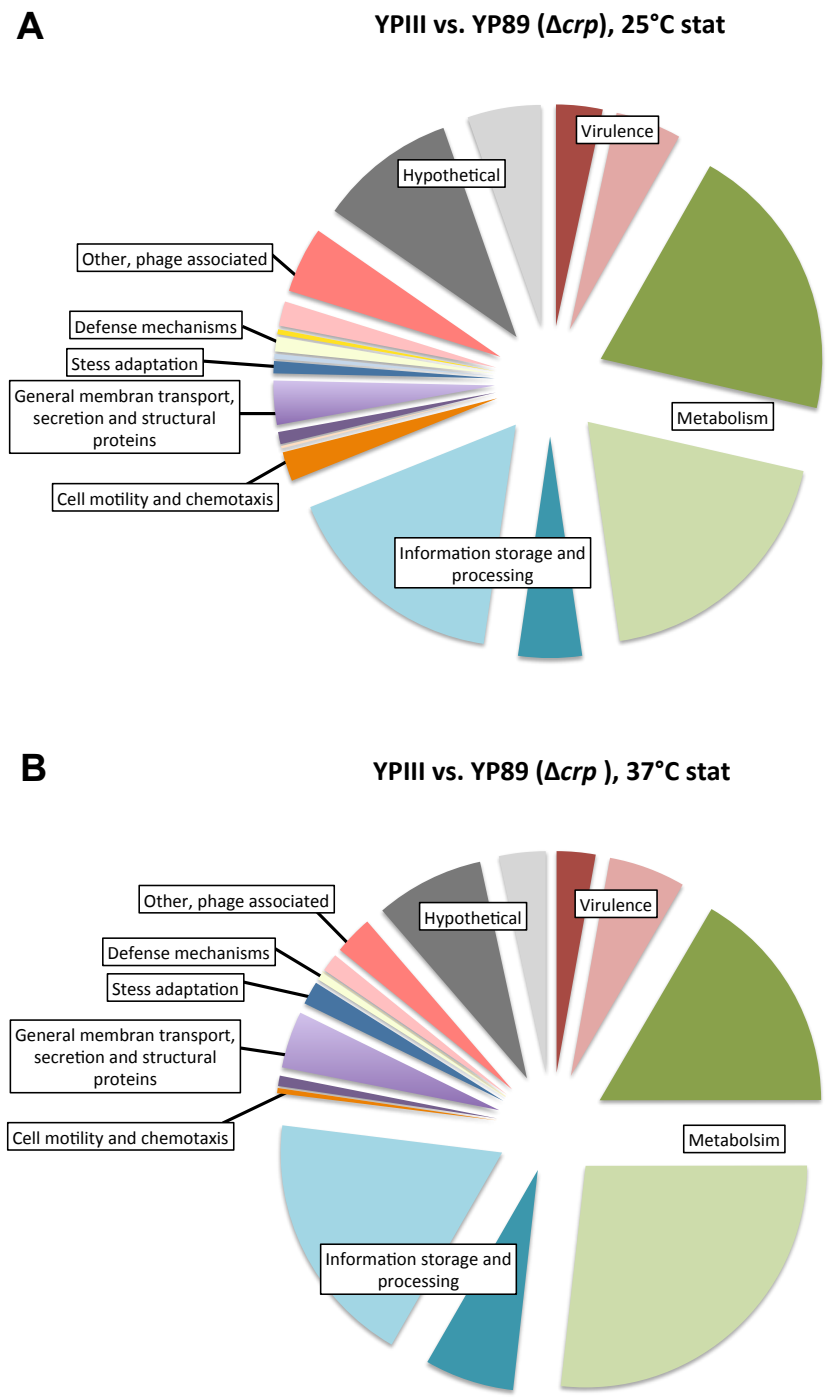


Figure 38: Pie chart illustrating the differentially regulated genes when the gene expression of the wild type was compared to the *Δcrp* deletion strain grown to the stationary growth phase. (A) Differentially regulated genes at 25°C and (B) at 37°C. Colors indicate different categories of gene function. Red: virulence-associated genes, green: metabolism-associated genes, turquoise: information storage and processing, orange: information storage and processing, orange: Cell motility and chemotaxis-associated, purple: general membrane transport, secretion and structural proteins, blue: stress adaptation, yellow: defense mechanisms, rosé: other, phase associated, grey: hypothetical proteins. Light colors indicate the number of upregulated genes while dark colors indicate downregulated genes.

When the gene expression in the wild type strain was compared to the *crp* deletion strain grown at 25°C during stationary growth, mostly genes associated with energy production and conservation, metabolism, and translation were influenced. Especially, genes involved in energy production and conservation (4 % of all regulated genes), amino acid metabolism (7 % of all regulated genes) and carbohydrate metabolism were downregulated (5 % of all regulated genes). The major groups of upregulated genes were associated with amino acid metabolism (7 % of all regulated genes), carbohydrate metabolism (4 % of all regulated genes) and translation (10 % of all regulated genes) (Figure 38 A).

Similar results were detected when the gene expression of the wild type and the Δ*crp* mutant grown at 37°C was compared. Mainly, genes involved in amino acid metabolism were downregulated (5 % each of all regulated genes). The majority of upregulated genes were associated with carbohydrate metabolism (4% of all regulated genes), amino acid metabolism (4 % each of all regulated genes), translational (9 % of all regulated genes) and energy production and processing (4 % of all regulated genes) (Figure 38 B). At both 25°C and 37°C approx. 5 % of all regulated genes were associated with virulence.

At 25°C the primary invasion factor *invA* was downregulated in the Δ*crp* mutant. Similar, its transcriptional regulator *rovA* was also downregulated, while the *rovA* repressor *rovM* was upregulated. The major regulator of the virulence genes of the ongoing infection *lcrF* was also downregulated. However, genes associated with Type VI secretion were upregulated at 25°C. Cell motility is inhibited by the deletion of *crp* at 25°C. In addition to *flhDC*, flagella motor proteins and genes associated with the assembly of flagella were downregulated. At 37°C genes associated with the T3SS were strongly upregulated. Furthermore, deletion of *crp* resulted in a downregulation of *flhDC* but not in the downregulation of motor and assembly associated genes.

At both temperatures the deletion of *crp* resulted in lower levels of TCA associated genes. Phosphotransferase systems were differentially regulated at 25°C and 37°C. Furthermore, at 25°C genes encoding for components of glycolysis were upregulated, while gluconeogenesis was induced at 37°C. Crp also influenced the expression of amino acid and nucleotide transporters. At 25°C the expression of several amino acid transporters was reduced, while an upregulation was detectable at 37°C. Genes of the nucleotide transporter and metabolism were upregulated at both temperatures.

This indicates, that Crp is important for gene expression of *Y. pseudotuberculosis* at 25°C and 37°C. In both conditions mainly amino acid and carbohydrate metabolism associated genes were differentially expressed compared to in the wild type grown at the same condition.

3.2.3 Determination of transcriptional start sites (TSS) in *Y. pseudotuberculosis* YPIII

The library preparation using TAP treatment (A. Nuss, unpublished) enriched the samples for 5'-ends, which allows the identification of TSS. To determine a TSS the following bioinformatic criteria had to be fulfilled: A sharp 5'-end with ≥ 20 reads and a ratio of 2:1 normalized read counts in relation to the sequence further upstream needed to be present (e.g. 10 reads upstream of 5'-end, 20 reads downstream). Thereby, a total number of 1164 TSS were identified, out of which 25 were located on the virulence plasmid pYV (Table S 11). In addition, the sequencing of TAP treated and untreated libraries allowed the discrimination between primary and processed transcripts, since TAP untreated samples are depleted for primary transcripts. Based on this, a depletion factor was calculated, which is the ratio of normalized read counts in TAP untreated vs. TAP treated conditions. TSS with a ratio < 0.5 were then considered as a real TSS while TSS with a higher ratio were determined as putative TSS. 939 start sites fulfilled the criteria to be classified as real TSS while 225 TSS were categorized as putative TSS (depletion factor ≥ 0.5). In total, one TSS was assigned to 814 genes, while 135 genes had two TSS, 20 genes three TSS, two genes four TSS, and two genes carried five TSS.

A representing gene locus is the *rovA* gene, which was extensively studied previously. Two TSS were reported 76 and 343 nts upstream of the translational start (Heroven *et al.*, 2004; Heroven and Dersch, 2006). Both TSS could be detected by Illumina sequencing (Figure 39). Further, the previously experimentally identified TSS of *udp*, *yscW* and *csrB* (Zolotukhina *et al.*, 2003; Heroven *et al.*, 2008; Böhme *et al.*, 2012) were also found by the Illumina sequencing reported here.

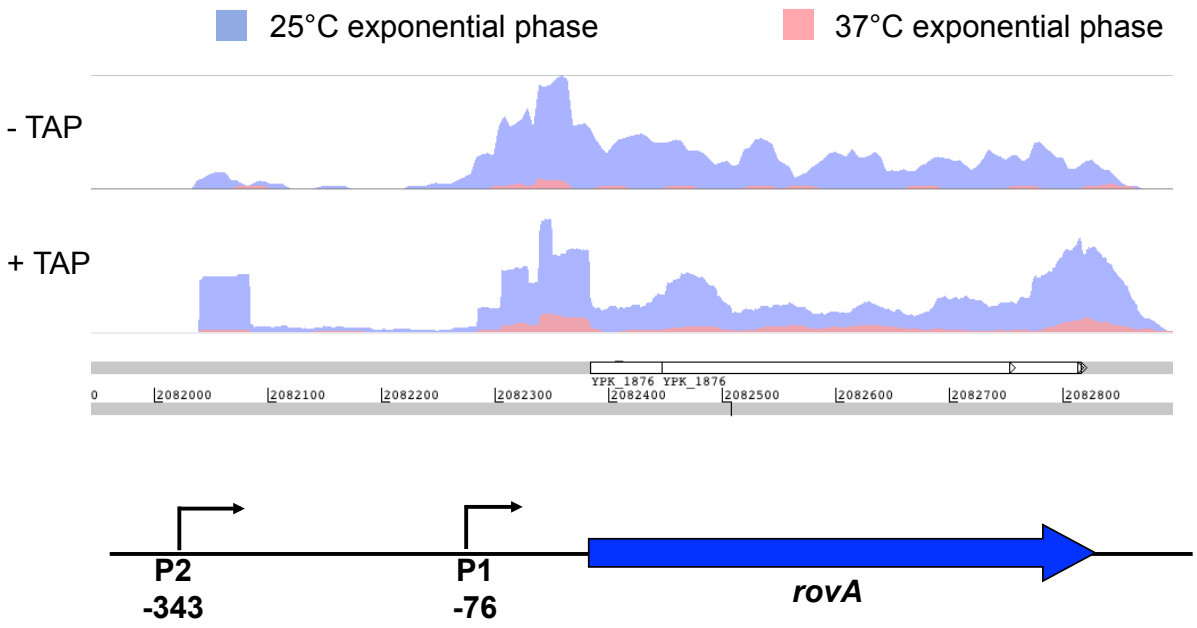


Figure 39: View of the Artemis genome browser showing the *rovA* locus. Illustrated is the *rovA* genomic region with the corresponding coverage in TAP untreated (upper panel) and TAP treated samples (lower panel). On the bottom the *rovA* promoter is schematically shown (Heroven *et al.*, 2004)**.**

The region between the transcriptional and translational start site is defined as 5' untranslated region (5' UTR). The TSS prediction performed here revealed a 5' UTR average length of 107 nts with a peak at 20-45 nts. 430 transcripts were identified to carry a 5' UTR longer then 100 nts, while 15 leaderless mRNA were detected (5' UTR shorter than 10 nts). 25 TSS were identified several nts downstream of the annotated translational start site. Additionally, the mapping of TSS was also carried out after sequencing of the Δ*crp* libraries. 48 TSS out of the 1164 TSS were detected only in the libraries sequenced from a Δ*crp* deletion strain. These TSS remained putative since only TAP treated Δ*crp* libraries were sequenced, which does not allow the calculation of the depletion factor.

Table 11: TSS of the indicated genes mapped by Illumina sequencing and 5' RACE. The indicated positions are in relation to the start codon of the gene.

Gene name	Position mapped in Illumina sequencing	Position mapped by 5' RACE
YPK_0152	-47	-47
YPK_1918	-65; -22	-64, -13
YPK_2072	-233; -48	-46

Gene name	Position mapped in Illumina sequencing	Position mapped by 5' RACE
YPK_2650	-39	-38
YPK_2676	-32; -44	-33; -44
YPK_3445	-63	-63
YPK_3761	-222; -48	-222, -49
YPK_4229	-113, -52	-110, -50
fliA	-200; -28	-172, -27
fliC	-65	-65

To validate the TSS of selected candidates by 5' RACE, total RNA was isolated from bacteria grown at 25°C and 37°C to the exponential and stationary growth phase. The TSS of ten candidates were verified by 5' RACE. Table 11 summarizes the results of the bioinformatic analysis and the results detected by 5' RACE. The TSS of YPK_0152, YPK_3445, and *fliC* was detected at the same position as predicted from the RNA-Seq approach, while the TSS of YPK_2650 was detected with one nts difference. The Illumina data predicted two TSS for the remaining six candidates, which could be confirmed for YPK_2676, YPK_3761, and YPK_4229. One of the TSS predicted for YPK_1918 and *fliA* was confirmed experimentally, while the second TSS was detected nine and 30 nts closer to the translational start site, respectively. Only one TSS of YPK_2072 was confirmed by 5' RACE.

In summary, the Illumina data described here allowed the mapping of TSS on a genome wide scale. Comparison of these data to already analyzed ORFs (e.g. *rovA, udp, csrB, yscW*) and 5' RACE experiments confirmed these data.

3.2.4 Crp binding site prediction and validation

The Crp regulon is well characterized in *E. coli* and *Y. pestis* (Zheng *et al.*, 2004; Zhan *et al.*, 2008). However, these studies focused on the identification of Crp-dependent ORFs. Out of the 163 sRNAs identified by Illumina sequencing, 91 were found to be Crp dependent. Ten of these sRNAs were only detectable after sequencing of the Δ*crp* libraries. This indicates, that Crp acts as a global regulator on sRNA expression. To gain first insights, if this effect is rather direct or indirect the upstream region of some of the Crp dependent sRNAs was analyzed with respect to the presents of potential Crp binding sites. To identify sRNAs, which are

directly controlled by Crp 200 nts upstream and 100 nts downstream of the predicted transcription start of the sRNAs were screened for the Crp consensus motif of *E. coli* (TGTGA-N_6-TCACA) allowing not more then two mismatches.

Seven *cis*-encoded antisense and 13 *trans*-encoded sRNAs were identified to harbor one putative Crp binding site (Table S 12). Two putative Crp binding sites were located in the upstream region of *trans*-encoded sRNAs (CsrB, YPK_transRNA_38), while YPK_transRNA_54 and YPK_transRNA_71 harbored three and four putative Crp binding sites, respectively. CyaR and Spot42 are the only sRNAs for which a direct Crp binding is described in *E. coli* (Papenfort *et al.*, 2008; Beisel and Storz, 2011). To confirm Crp binding to the regulatory region of other identified Crp-dependent sRNAs with potential Crp binding sites in their promoter region, ten sRNAs were tested for direct Crp binding using electromobility shift assays (EMSA).

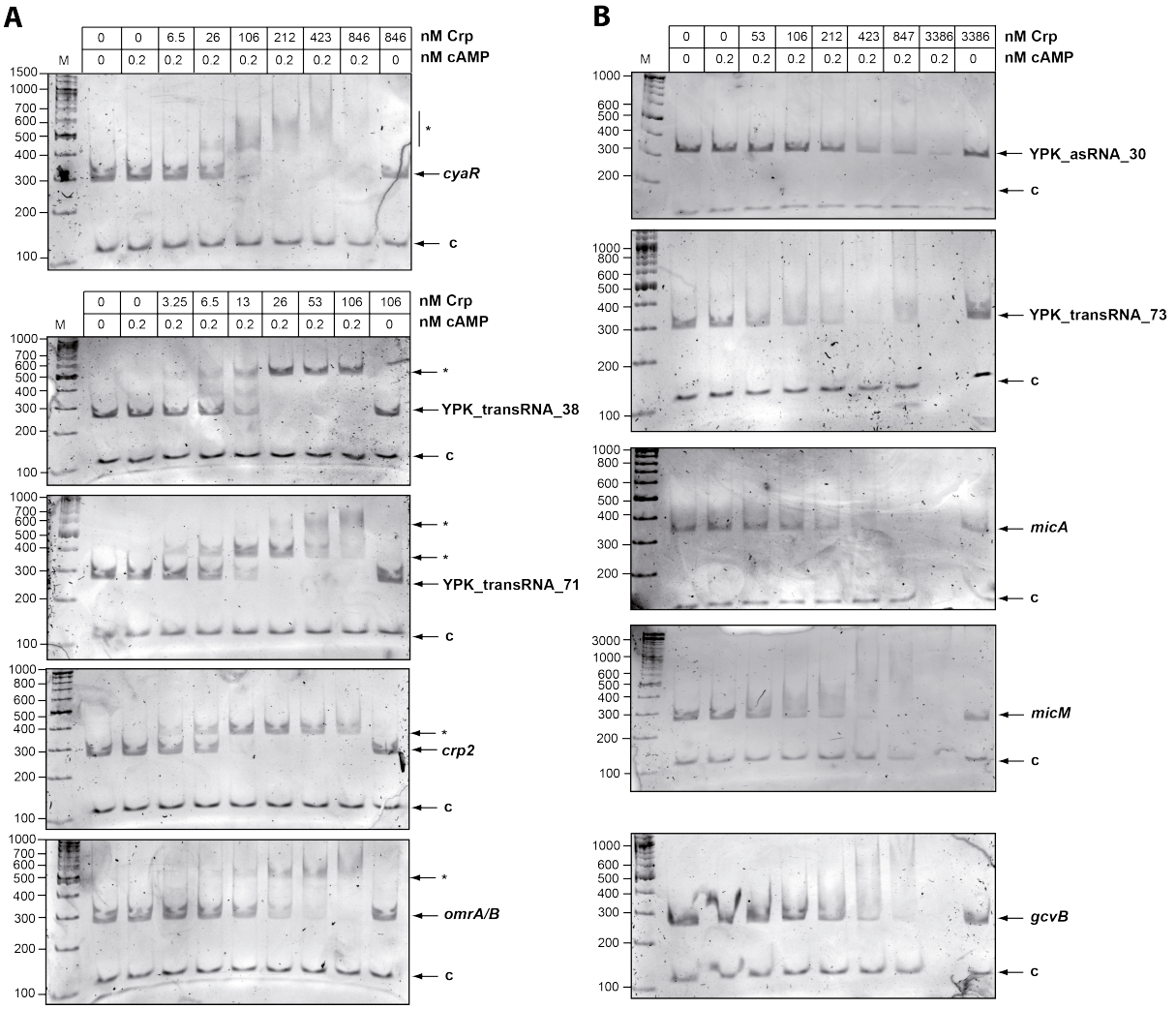


Figure 40: Interaction of Crp with the upstream regions of ten sRNAs for which a Crp binding site was predicted. 130 fmol of the respective DNA were incubated with increasing concentrations of Crp protein as well as 0.2 mM cAMP at 30°C for 20 min. A sample with the highest protein concentration without cAMP was used as negative control (right panel). Subsequently, the samples were separated on a native 4 % acrylamide/0.5 x TBE gels and stained with ethidium bromide. C indicates the control fragment, while * indicates the higher molecular weight protein-DNA complex. The corresponding molecular weight is indicated on the left. (A) Fragments that were specifically bound by Crp. (B) Fragments that were not specifically bound by Crp.

To analyze binding of the Crp protein to the upstream region of the sRNAs, Crp was overexpressed and purified. The DNA fragments were synthesized by PCR. Subsequently, in the presents of cAMP increasing concentrations of Crp protein were incubated with a control DNA fragment and the fragment of interest.

YPK_transRNA_38 was predicted to have two Crp binding sites, YPK_transRNA_71 was indicated to carry 4 Crp binding sites, *gcvB* was predicted to carry no Crp binding site, and the remaining seven candidates were predicted to carry one Crp binding site. Crp was found

to specifically interact with five of these DNA fragments (Figure 40 A). The binding of Crp to the *cyaR* regulatory region was already characterized in *E. coli* and was used as a positive control (Papenfort *et al.*, 2008). Additionally, direct binding of Crp to the upstream region of *omrA/B,* YPK_transRNA_38, and YPK_transRNA_71 was observed. The upstream region of Crp2 was also chosen for EMSA and specific binding of Crp to its upstream region was detected.

First binding of Crp to the promoter region of *cyaR* was observed at 26 nM Crp protein while complete binding was detectable at 106 nM Crp protein. Similar results were detected for the upstream region of *omrA/B.* In contrast, the binding affinity to YPK_transRNA_38, YPK_transRNA_71, and crp2 was much higher. Initial binding was detectable at 3.25 nM Crp, while a complete binding was observed at 26 and 13 nM Crp protein, respectively.

Crp did not specifically bind the upstream regions of YPK_asRNA_30, YPK_transRNA_73, *micA*, *micM*, and *gcvB* or shows a very low affinity, even though much high protein concentrations were used (Figure 40 B). Only at very high protein concentration Crp forms an undefined complex with the promoter regions of these five genes and the control fragment. This indicates non-specific binding of Crp to DNA due to very high protein concentrations.

Taken together, the binding of Crp to the *cyaR* promoter region was confirmed in *Y. pseudotuberculosis*. Additionally, Crp binding to four newly identified sRNA promoter regions was confirmed, indicating that Crp regulates the expression of several sRNAs.

3.3 Influence of sRNAs on *Yersinia* virulence

In *Y. pseudotuberculosis* the impact of only a few sRNAs on virulence were analyzed. In this study two sRNAs were analyzed with respect to their influence on virulence using the mouse model. The sRNAs MicA and CyaR are well characterized in *E. coli* and *Salmonella*. In addition to *nadE*, in *E. coli* CyaR targets *ompX* and *luxS* (De Lay and Gottesman, 2009). In *Yersinia ompX* encodes an Ail homologue, which is essential for adhesion and serum resistance (Bartra *et al.*, 2008; Kolodziejek *et al.*, 2010). The *luxS* gene encodes a quorum sensing system and influences biofilm formation (Bobrov *et al.*, 2007), which is essential for *Y. pestis* to colonize the flea and be efficiently transmitted to the human host. Deletion of *luxS*

resulted in higher susceptibility to oxidative stress (Chouikha and Hinnebusch, 2012; Yu *et al.*, 2013). MicA represses *ompA* expression by binding to the SD sequence, which is necessary for *Y. pseudotuberculosis* to survive in macrophages (Udekwu *et al.*, 2005; Bartra *et al.*, 2012). Both sRNAs were recently shown to be highly expression in *Y. pestis* during infection (Yan *et al.*, 2013).

To investigate the impact of these two sRNAs on the virulence of *Y. pseudotuberculosis* the mouse infection model was used to compare the survival and colonization of host tissue by the *Y. pseudotuberculosis* wild type strain IP32953 and the isogenic *cyaR* and *micA* mutant. Groups of five mice were infected orally with 1 x 10^8 bacteria. Their survival was monitored for 11 days and the date of death was recorded (Figure 41 A). Mice infected with the wild type strain as well as the mutant strains showed signs of infection (e.g. weight loss) and died 6-11 days post infection.

Additionally, the number of bacteria present in the Peyer's Patches (PP), the mesenterial lymph nodes (MLN), the liver, and the spleen was determined four days post infection (Figure 41 B). Similar numbers of wild type and mutant bacteria were detected in all organs, indicating that a deletion of neither *cyaR* nor *micA* has an influence on the virulence of *Y. pseudotuberculosis*.

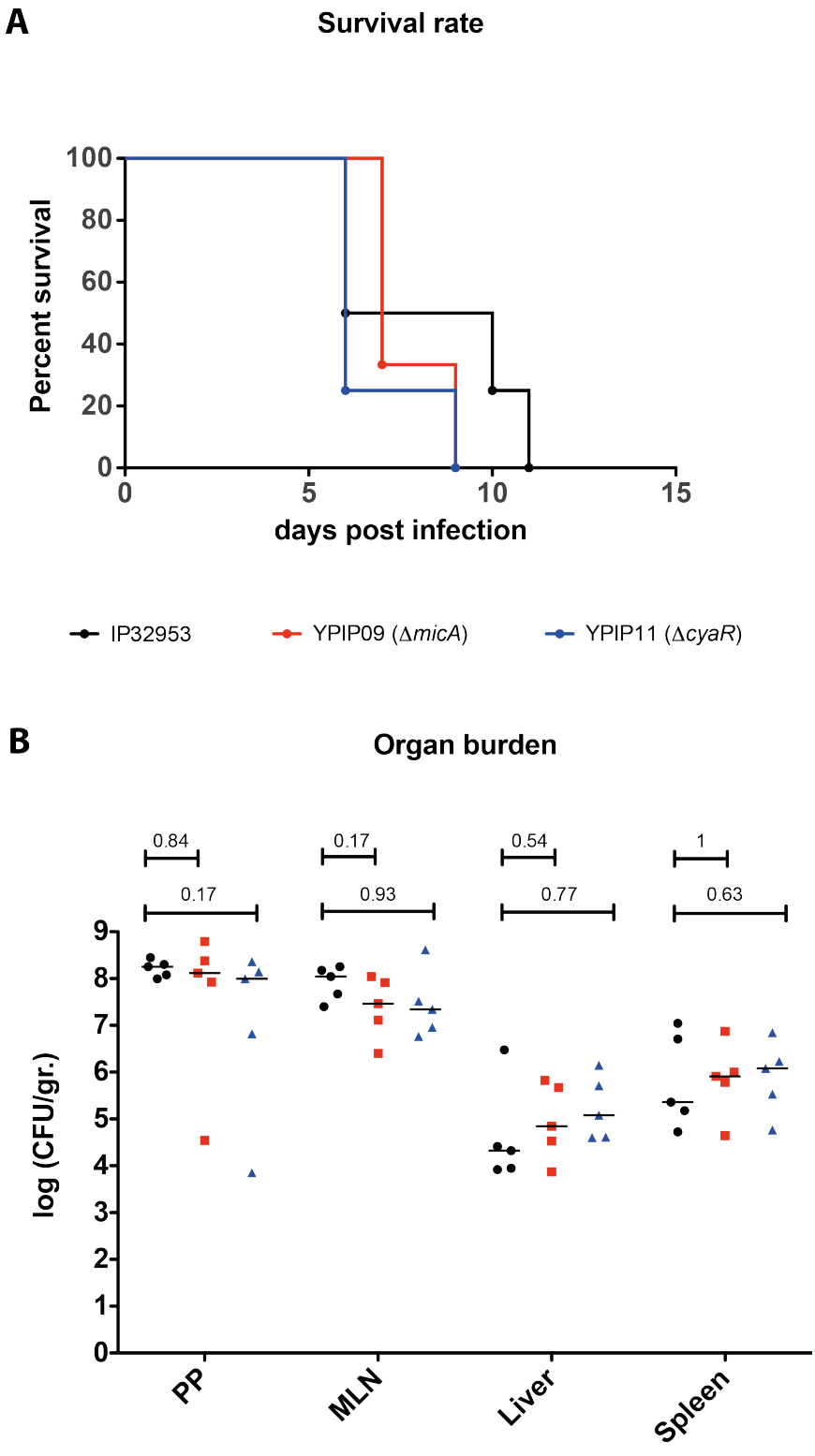


Figure 41: Influence of CyaR and MicA on the virulence in mice. Five mice were infected orally with one bacterial strain and a dose of 1 x 10^8 bacteria. The body weight was monitored two days before infection and 11 days post infection. Mice that lost more than 30 % of their body weight were killed. The organ burden was analyzed four days post infection. The p-value was calculated by the Students unpaired t-test and is indicated in (B). (A) Survival of mice after infection with the indicated strains. (B) Organ burden of mice infected with the indicated strains four days post infection.

3.4 Function and regulation of the RNA chaperon Hfq in *Y. pseudotuberculosis*

3.4.1 Regulation of *hfq* expression

The regulatory cascade influencing *hfq* expression is characterized in *E. coli*. Here, the *hfq* gene is transcribed from three independent promoters, out of which two are controlled in a σ^{70} dependent manner, while the third promoter is controlled by the heat shock sigma factor σ^{32} (Tsui *et al.*, 1996). In *Y. pseudotuberculosis* YPIII, all three promoters were found by Illumina sequencing reported here.

Additionally, in *E. coli* the Crp-cAMP complex was found to inhibit *hfq* expression by direct binding to its promoter region. Further, CsrA was identified to influence the expression of *hfq* in a posttranscriptional manner. Binding of CsrA to the mRNA blocks the RBS, which leads to the degradation of the mRNA (Vecerek *et al.*, 2005; Baker *et al.*, 2007; Lin *et al.*, 2011). Autoregulation of *hfq* in a negative manner was also reported (Vecerek *et al.*, 2005).

In *Y. pseudotuberculosis* only functional studies of *hfq* were carried out, but the expression of *hfq* was not analyzed. Therefore, this study focused on the regulation of *hfq* expression.

3.4.1.1 Temperature and growth phase control

In order to analyze the impact of temperature and the growth phase on the expression of *hfq*, western blot analysis and β-galactosidase activity assays were carried out.

The *hfq* expression was first monitored by β-galactosidase activity assays. Therefore, the *lacZ* gene was fused as a translational fusion to the promoter region of *hfq* carrying the first 63 nts of the *hfq* gene, which were reported to be essential for autoregulation in *E. coli* (Vecerek *et al.*, 2005). Two constructs were generated, one carrying the regulatory region of P3 and one carrying the regulatory regions of P2 and P3 (Figure 42). In *E. coli* P1 was identified as a heat shock promoter (Tsui *et al.*, 1996) and was therefore not include in the following analysis. The respective plasmids were transformed in the YPIII wild type strain and the *hfq-lacZ* expression was measured after growth at 25°C or 37°C to the exponential or stationary growth phase.

The highest β-galactosidase activity of the P3 construct was measured at 25°C and 37°C in stationary growth. The expression at 37°C in the stationary growth phase was slightly

elevated compared to the expression at 25°C in stationary growth. In the exponential growth phase the β-galactosidase activity was approx. 2 fold lower than in the stationary growth phase. Similar results were detected for the P2+P3 promoter construct. The highest expression was detectable in the stationary growth phase at both temperatures. In contrast to the P3 construct the expression of the P2+P3 construct was elevated at 37°C, when the bacteria were grown to the exponential growth phase. The expression under this condition was similar to that in the stationary growth phase. This indicates, that the transcription of *hfq* is regulated in a growth phase- and temperature-dependent manner (Figure 42 A).

Hfq protein levels were also dependent on the growth phase as well as on temperature. Consistent with the reporter fusion, the protein expression was highest in the stationary growth phase. After growth in the exponential growth phase slightly higher Hfq levels were detectable at 37°C than at 25°C, indicating a temperature-dependent expression (Figure 42 B).

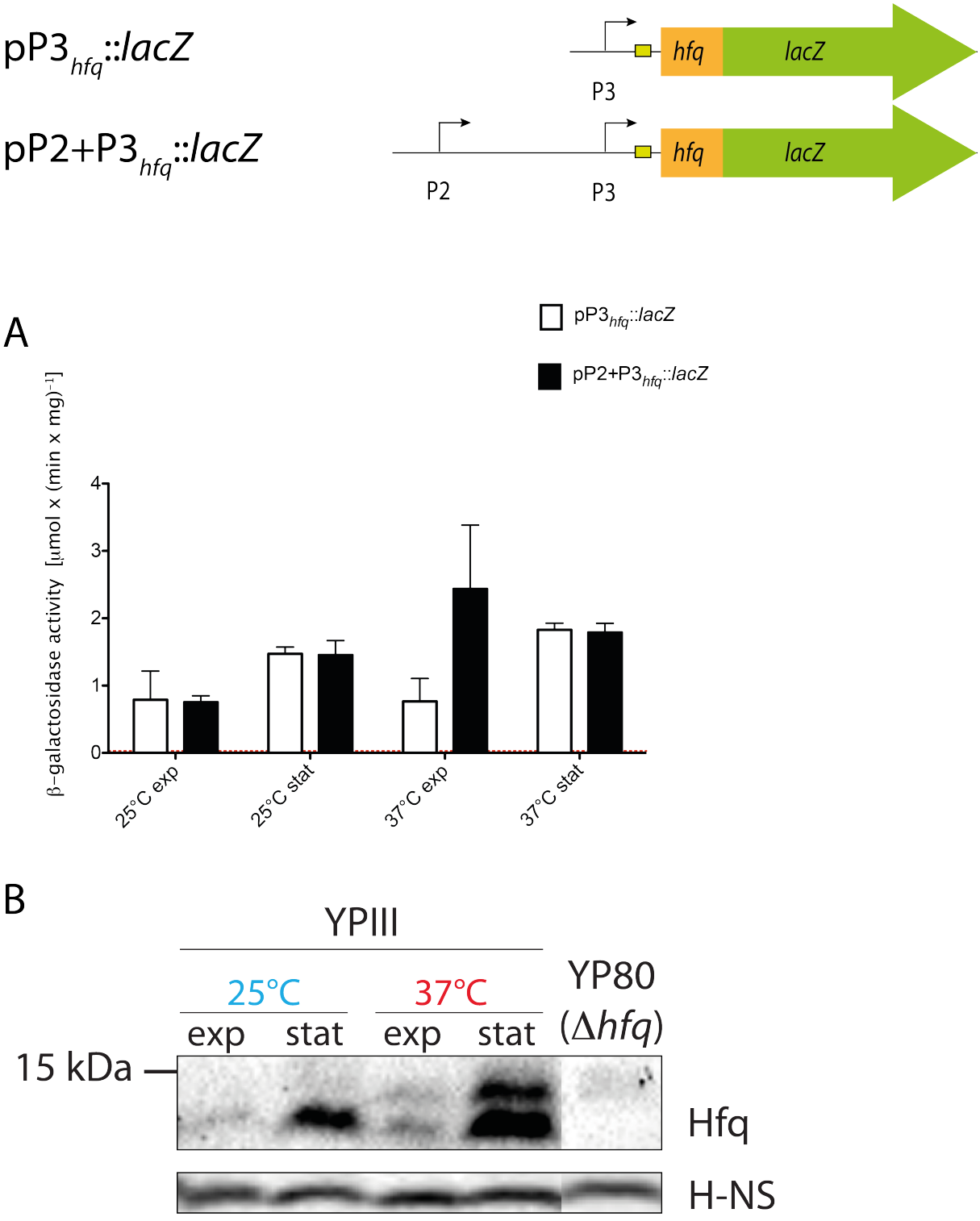


Figure 42: Temperature- and growth phase-dependent Hfq expression. (A) The indicated constructs were transformed in the YPIII strain the *hfq-lacZ* expression was determined after growth in LB medium at 25°C or 37°C in the exponential or stationary growth phase. The error bars indicates the standard deviation of three independent cultures, each measured in duplicates. The β-galactosidase activity is given in [µmol x (min x mg) $^{-1}$]. The red line indicates the empty vector control. (B) Hfq protein levels after growth in LB medium at 25°C or 37°C in the exponential growth phase. Bacterial cells were lysed and western blot analysis was carried out. H-NS served as loading control.

3.4.1.2 Influence of Crp and CsrA on *hfq* expression in *Y. pseudotuberculosis* YPIII

In *E. coli* the expression of *hfq* is well characterized and it was shown that Crp and CsrA have a negative effect on *hfq* expression (Vecerek *et al.*, 2005; Baker *et al.*, 2007; Lin *et al.*, 2011). The study reported here addressed the question how the *hfq* expression is regulated in *Y. pseudotuberculosis* and if Crp and CsrA have the same effect as in *E. coli*.

To analyze the impact of both proteins on *hfq* expression, western blot analysis and β-galactosidase activity assays were performed. The *lacZ*-reporter plasmids were transformed in the wild type (YPIII), the Δ*csrA* (YP53), and Δ*crp* (YP89) strain. β-galactosidase activity assays were carried out as described in the previous chapter (see section 3.4.1.1). The Hfq protein levels were analyzed in the wild type (YPIII), the Δ*csrA* (YP53), and Δ*crp* (YP89). All strains were transformed with the empty vector pACYC184 (indicated as YPIII pV, YP53 pV, YP89 pV in Figure 43). For complementation the plasmid pACYC184-*csrA+* (pAKH56) was transformed in the Δ*csrA* strain (YP53 p*csrA+*), while pACYC184-*crp*+ (pAKH37) was transformed in the Δ*crp* strain (YP89 p*crp+*).

Figure 43 illustrates the results of the β-galactosidase activity assays. Deletion of *crp* as well as *csrA* had no influence on the *lacZ* expression of the construct carrying the promoter region up to P3. Additionally, the activity of the construct carrying the promoter region up to P2 was not affected (Figure 43 A). Hfq protein levels detected by western blotting were not altered in a Δ*csrA* or Δ*crp* mutant (Figure 43 B) indicating that in contrast to *E. coli* CsrA and Crp do not influence the expression of *hfq* in *Y. pseudotuberculosis*.

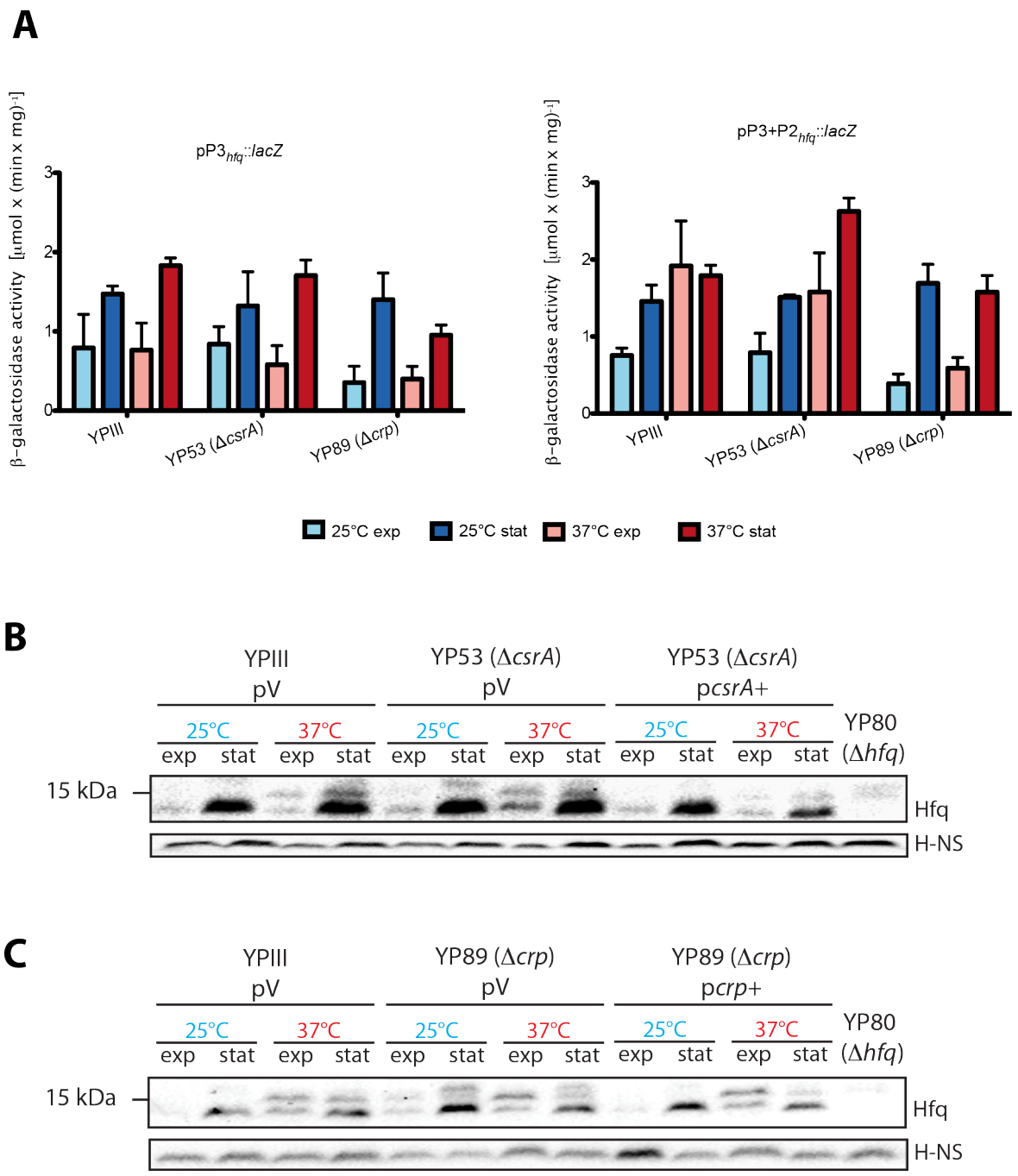


Figure 43: Influence of Crp and CsrA on the expression of *hfq*. (A) The indicated constructs were transformed in the YPIII, YP53, and YP89 strain and the *hfq-lacZ* expression was determined after growth in LB medium at 25°C or 37°C the exponential or stationary growth phase. The error bars indicate the standard deviation of three independent cultures, each measured in duplicates. The P_{hfq}*::lacZ*-activity is given in [µmol x (min x mg) $^{-1}$]. (B), (C) Hfq protein levels after growth in LB medium at 25°C or 37°C in the exponential growth phase in the YPIII carrying the empty vector control or the YP53/YP89 strain carrying either the empty vector control or the respective complementation plasmid. Bacterial cells were lysed and western blot analysis was carried out. H-NS served as loading control.

3.4.2 Function of Hfq in *Y. pseudotuberculosis* YPIII

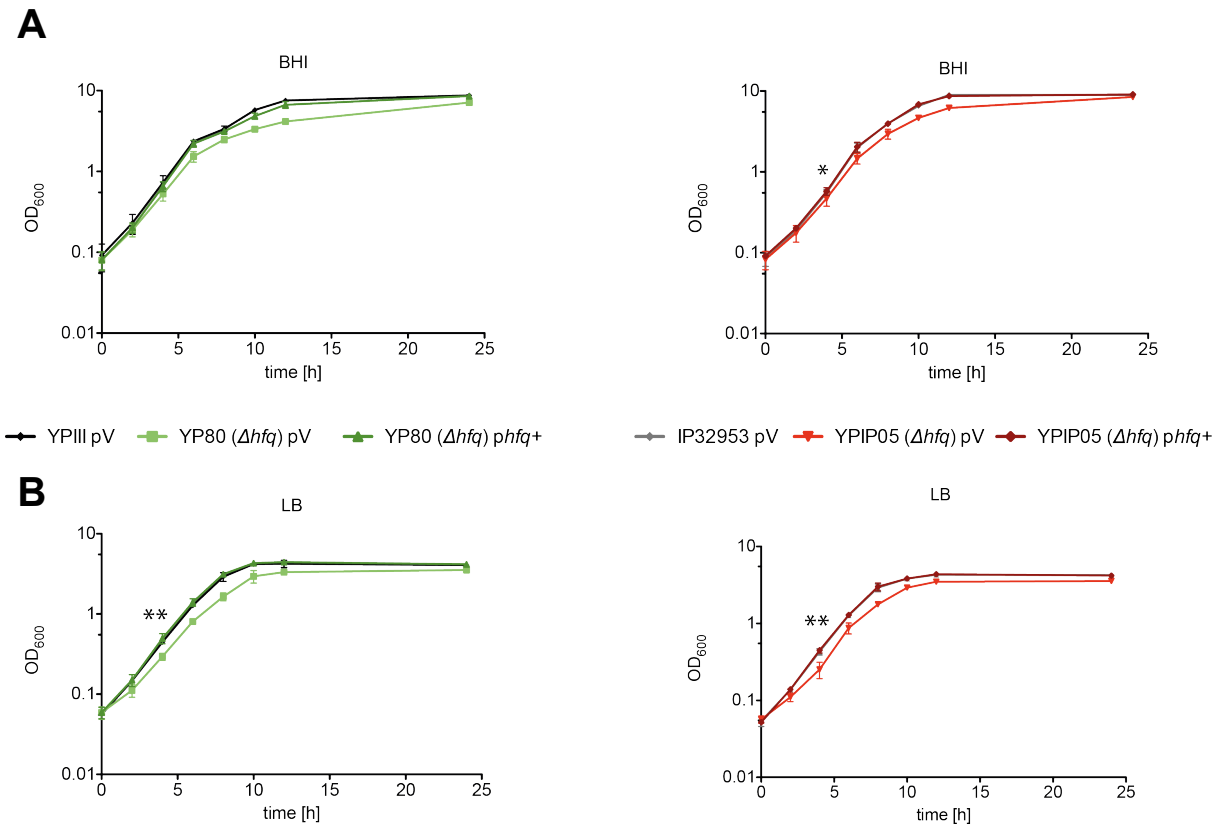
The RNA chaperone Hfq is present in many bacteria and the functionality of many sRNAs is Hfq-dependent, because Hfq enhances the RNA-RNA interaction between an sRNA and its target mRNA (Wagner, 2013). Moreover, Hfq binding can influence the stability of sRNAs in a positive or negative manner (Vogel and Luisi, 2011). In this study, the expression of several newly identified sRNAs was dependent on the RNA chaperone suggesting an important role for Hfq and sRNAs in *Y. pseudotuberculosis* YPIII. In fact, in the mouse model a *Y. pseudotuberculosis* Δ*hfq* strain was faster cleared and a *Y. pestis* Δ*hfq* strain showed reduced virulence (J Geng *et al.*, 2009; Schiano *et al.*, 2010). Additionally, the deletion in both pathogens resulted in higher sensitivity to oxidative stress and lower survival within macrophages, while the growth appeared severely impaired in the *Y. pestis* Δ*hfq* strain (J Geng *et al.*, 2009; Schiano *et al.*, 2010). This study aimed to elucidate the role of Hfq in the *Y. pseudotuberculosis* clinical isolate YPIII.

3.4.2.1 Effect of Hfq on the growth of *Y. pseudotuberculosis* YPIII and IP32953

Previous studies indicated that a deletion of the *hfq* gene in *Y. pestis* affects its growth behavior. These studies indicated that a *Y. pestis* Δ*hfq* mutant shows different growth behavior in BHI and TMH medium. Further, the growth of Δ*hfq* mutants in different wild type backgrounds (Kim, CO92, Kuma) was altered differently (J Geng *et al.*, 2009; Bai *et al.*, 2010). In *Y. pseudotuberculosis* IP32953 no growth defect was reported but preliminary data indicate that the YPIII strain might show a growth defect (Schiano *et al.*, 2010; Heroven, unpublished). Therefore, this study aimed to compare the growth of the clinical isolates YPIII and IP32953 in different growth media.

BHI, LB, and DMEM medium was used. BHI medium is a full medium containing high amounts of all nutrients, while LB medium contains lower amounts of nutrients. DMEM medium is a defined medium with glucose and pyruvate as only available carbon source. For complementation the *hfq* gene under its native promoters was cloned in the pHSG575 plasmid. Subsequently, the empty vector control was transformed in the wild type strains YPIII and IP32953 and their isogenic mutant strains Δ*hfq* YP80 and YPIP05. The complementation plasmid was transformed into the Δ*hfq* mutant strains YP80 and YPIP05.

Fresh medium was inoculated with over night cultures of the two wild type strains carrying the empty vector control (YPIII pV, IP32953 pV), their respective *hfq* mutants carrying the empty vector control (YP80 pV, YPIP05 pV), or the Δ*hfq*/pHSG575-*hfq+* strains (YP80 p*hfq+,* YPIP05 p*hfq+*). The start OD_{600} was inoculated to 0.05 and growth at 25°C was monitored for 24 h (Figure 44 A and B).



C

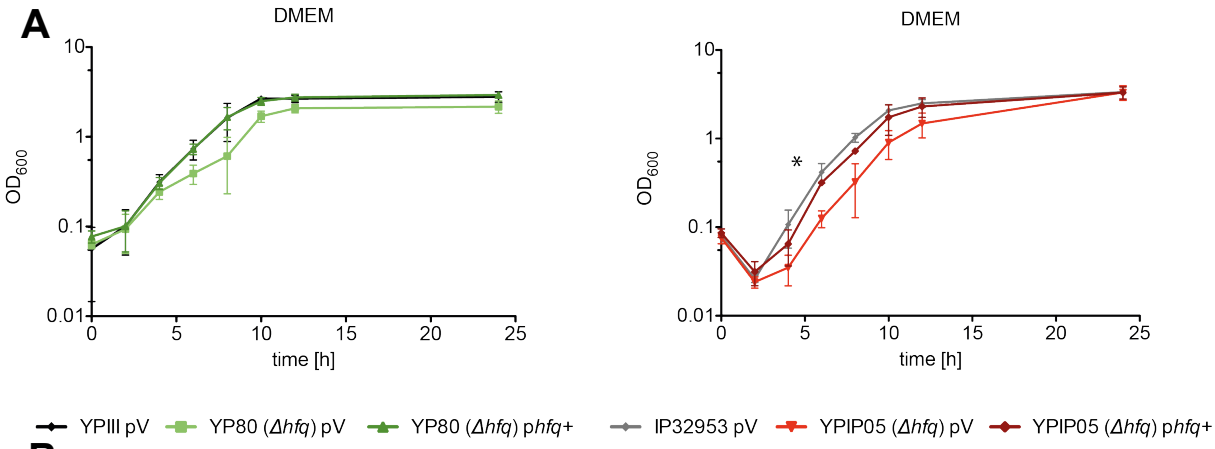
	Growth rate [h^{-1}]	Doubling time [h]		Growth rate [h^{-1}]	Doubling time [h]
BHI			**BHI**		
YPIII pV	0.236	1.27	IP32953 pV	0.227	1.34
YP80 *(Δhfq)* pV	0.214	1.42	YPIP05 *(Δhfq)* pV	0.207	1.46
YP80 *(Δhfq)* p*hfq+*	0.239	1.26	YPIP05 *(Δhfq)* p*hfq+*	0.223	1.35
LB Medium			**LB Medium**		
YPIII pV	0.214	1.41	IP32953 pV	0.219	1.37
YP80 *(Δhfq)* pV	0.194	1.55	YPIP05 *(Δhfq)* pV	0.2	1.51
YP80 *(Δhfq)* p*hfq+*	0.219	1.37	YPIP05 *(Δhfq)* p*hfq+*	0.22	1.37

Figure 44: Growth of YPIII and IP32953 and their respective *Δhfq* mutant strains in (A) BHI and (B) LB medium at 25°C. Fresh LB or BHI medium was inoculated with the respective strain to a start OD_{600} of 0.05 and the growth was monitored for 12 h every 2 h and after 24 h. Growth was monitored at 25°C for three independent cultures of each strain. The error bars indicate the calculated standard deviation at reach time point. The growth rate was calculated in exponential growth and compared between the different strains. Based on the Students unpaired t-test * represents a p-values of 0.05, ** represents p-values below 0.01. Time against OD_{600} was plotted in a semilogarithmic scale**.** (C) Growth rates and doubling time of all strains.

The growth rate of all strains was calculated during exponential growth. In all three media Δ*hfq* bacteria exhibit a statistically relevant growth defect. In BHI an LB medium the respective Δ*hfq* mutant strains grew slower than the wild type strains (Figure 44 C). Interestingly, an even stronger growth defect was observed during growth in DMEM medium (Figure 45 C). Ectopic expression of *hfq* fully restored these growth defects.

These data indicate that deletion of *hfq* in *Y. pseudotuberculosis* YPIII and IP32953 affects growth especially in medium with low nutrients. Growth of Δ*hfq* mutant strains in the YPIII and IP32953 background is attenuated to the same extend. The doubling time of the Δ*hfq* mutant strains grown in DMEM medium was more severely affected than after growth in LB and BHI medium.

A



B

	Growth rate [h^{-1}]	Doubling time [h]		Growth rate [h^{-1}]	Doubling time [h]
DMEM			**DMEM**		
YPIII pV	0.202	1.57	IP32953 pV	0.264	1.14
YP80 *(Δhfq)* pV	0.132	2.44	YPIP05 *(Δhfq)* pV	0.178	1.76
YP80 *(Δhfq)* p*hfq+*	0.205	1.49	YPIP05 *(Δhfq)* p*hfq+*	0.228	1.33

Figure 45: Growth of YPIII and IP32953 and their respective *Δhfq* mutant strains in DMEM medium at 25°C. (A) Fresh DMEM medium was inoculated with the respective strain to a start OD_{600} of 0.05 and the growth was monitored for 12 h every 2 h and after 24 h. Growth was monitored at 25°C for three independent cultures of each strain. The error bars indicate the calculated standard deviation at reach time point. The growth rate was calculated in exponential growth and compared between the different strains. Based on the Students unpaired t-test * represents a p-values of 0.05, ** represents p-values below 0.01. Time against OD_{600} was plotted in a semilogarithmic scale. (B) Growth rates and doubling time of all strains.

3.4.2.2 Impact of Hfq in *Y. pseudotuberculosis* YPIII during environmental stress

The expression of many sRNAs is dependent on different environmental signals. sRNAs such as RyhB, GlmY, GlmZ, MicM, CyaR, Spot42, are involved in pathways contributing to the iron metabolism, cell wall synthesis, regulation of outer membrane protein production, or catabolite repression (Massé and Gottesman, 2002; Møller *et al.*, 2002; Kalamorz *et al.*, 2007; Papenfort *et al.*, 2008; Reichenbach *et al.*, 2008). Therefore, the importance of Hfq on growth during osmotic stress, pH stress, limited oxygen, and oxidative stress was examined. Since Crp and CsrA did not influence the expression of *hfq* in *Y. pseudotuberculosis* YPIII these environmental signals might also indicate other crucial factors influencing *hfq* expression. Therefore, the Hfq protein levels were examined under the indicated

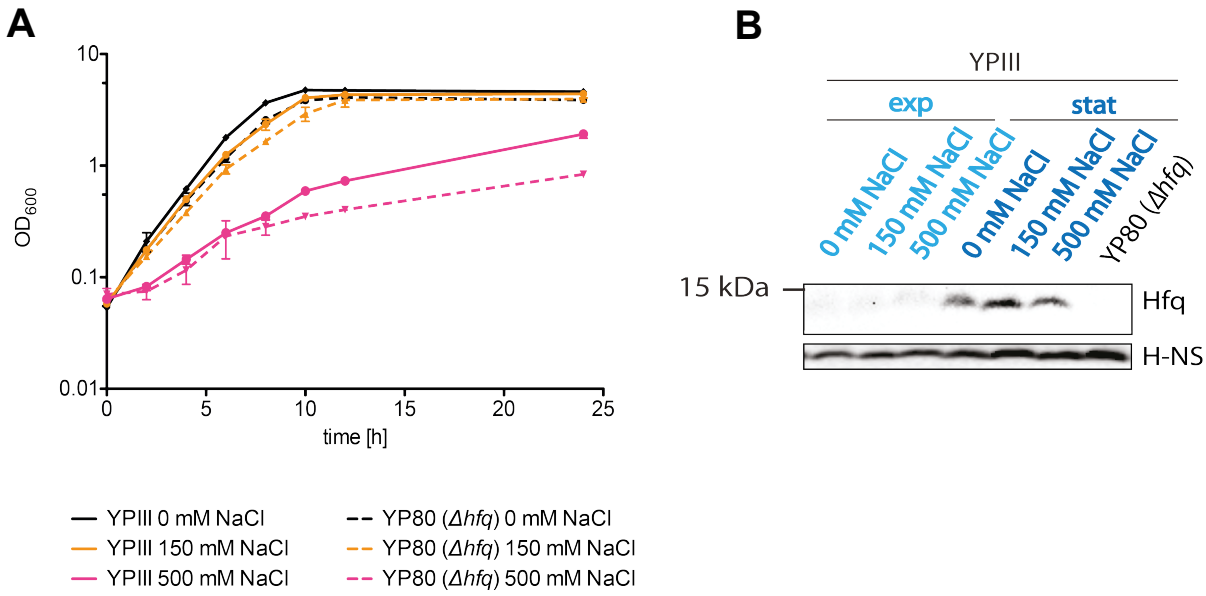
environmental stress conditions. If not indicated differently, bacteria were grown at 25°C to the exponential or stationary growth phase under the indicated stress conditions. Subsequently, the bacterial cells were lysed and western blot analysis was performed.

Osmotic stress

Osmotic stress was introduced by the addition of different NaCl concentrations to the growth medium. LB medium was supplemented with either 0, 150 mM, or 500 mM NaCl and inoculated from over night cultures of the YPIII strain and the isogenic *Δhfq* mutant strain to a start OD_{600} of 0.05. The growth was monitored at 25°C for 24 h.

No significant differences between the wild type and the *Δhfq* mutant strain could be observed (Figure 46 A). The growth of the wild type in medium supplemented with 150 mM was slightly slower compared to growth in normal LB medium. The doubling time of the Δ*hfq* mutant strain was again slightly slower compared to the wild type grown in the same stress condition. This reduction in growth is similar to the differences when wild type and Δ*hfq* mutant were grown at non-stress conditions. The addition of 500 mM NaCl led to a 2 fold slower growth of the wild type compared to the untreated control. The growth of the Δ*hfq* mutant was not altered further. Western blot analysis showed, that Hfq protein levels were similar under low and high salt concentrations.

This indicates that Hfq is not involved in the response to osmotic stress.



	Growth rate [h^{-1}]	Doubling time [h]
YPIII		
0 mM NaCl	0.206	1.46
150 mM NaCl	0.186	1.62
500 mM NaCl	0.104	2.87

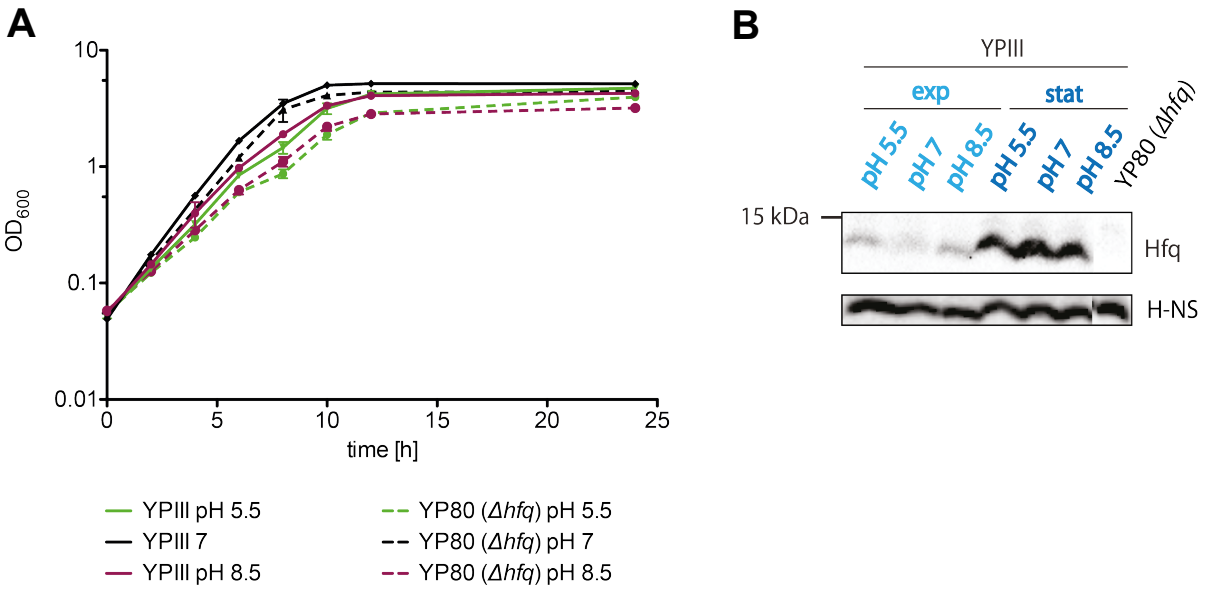
	Growth rate [h^{-1}]	Doubling time [h]
0 mM NaCl		
YPIII	0.206	1.46
YP80 *(Δhfq)*	0.192	1.56
150 mM NaCl		
YPIII	0.186	1.62
YP80 *(Δhfq)*	0.171	1.76
500 mM NaCl		
YPIII	0.104	2.87
YP80 *(Δhfq)*	0.095	3.20

Figure 46: Influence of increasing NaCl concentrations on the growth of *Y. pseudotuberculosis*. Fresh medium supplemented with either 0 mM, 150 mM, or 500 mM NaCl was inoculated with the respective strain to a start OD_{600} of 0.05 and the growth was monitored for 12 h every 2 h and after 24 h. Growth was monitored at 25°C for three independent cultures of each strain. The error bars indicate the calculated standard deviation at reach time point. The growth rate was calculated in exponential growth and compared between the different strains. Time against OD_{600} was plotted in a semilogarithmic scale. (A) Growth of YPIII and YP80 (*Δhfq*) under osmotic stress. LB medium was supplemented with the indicated amounts of NaCl and growth was monitored every 2 h. (B) Hfq levels in the wild type strain under osmotic stress. Samples were taken in the exponential or stationary growth phase. (C) Growth rates and doubling time of all strains.

pH stress

To monitor the influence of pH on the growth of the wild type and the Δ*hfq* mutant LB medium was buffered with MES or MOPS and the pH was adjusted to 5.5, 7, or 8.5. Fresh medium was inoculated from over night cultures of the YPIII strain and the isogenic *Δhfq* mutant strain to a start OD_{600} of 0.05. The growth was monitored at 25°C over 12 h every 2 h and after 24 h (Figure 47).

Both acidic and alkaline pH affected the doubling time of the wild type. The growth of the *Δhfq* mutant was slower but did not differ from the growth defect detectable in LB medium. Hfq protein levels were not altered upon growth in different pH (Figure 47 B). Taken together, Hfq seems not to be involved in the response to pH stress.



C

	Growth rate [h^{-1}]	Doubling time [h]		Growth rate [h^{-1}]	Doubling time [h]
YPIII			**pH 5.5**		
			YPIII	0.172	1.76
pH 7	0.214	1.4	YP80 *(Δhfq)*	0.141	2.13
pH 5.5	0.172	1.76			
pH 8.5	0.185	1.63	**pH 7**		
			YPIII	0.214	1.4
			YP80 *(Δhfq)*	0.214	1.41
			pH 8.5		
			YPIII	0.185	1.63
			YP80 *(Δhfq)*	0.155	1.93

Figure 47: Influence of different pH on *Y. pseudotuberculosis*. LB medium was buffered with MES or MOPS and the indicated pH was adjusted. Fresh medium was inoculated with the respective strain to a start OD_{600} of 0.05 and the growth was monitored for 24 h. Growth was monitored at 25°C for three independent cultures of each strain. The error bars indicate the calculated standard deviation at reach time point. The growth rate was calculated in exponential growth and compared between the different strains. Time against OD_{600} was plotted in a semilogarithmic scale. (A) Growth of YPIII and YP80 (*Δhfq*) and LB medium with different pH. (B) Hfq protein levels in YPIII grown in LB medium with pH 5.5, pH 7 and pH 8.5. Samples were taken in the exponential growth phase. (C) Growth rates and doubling time of all strains.

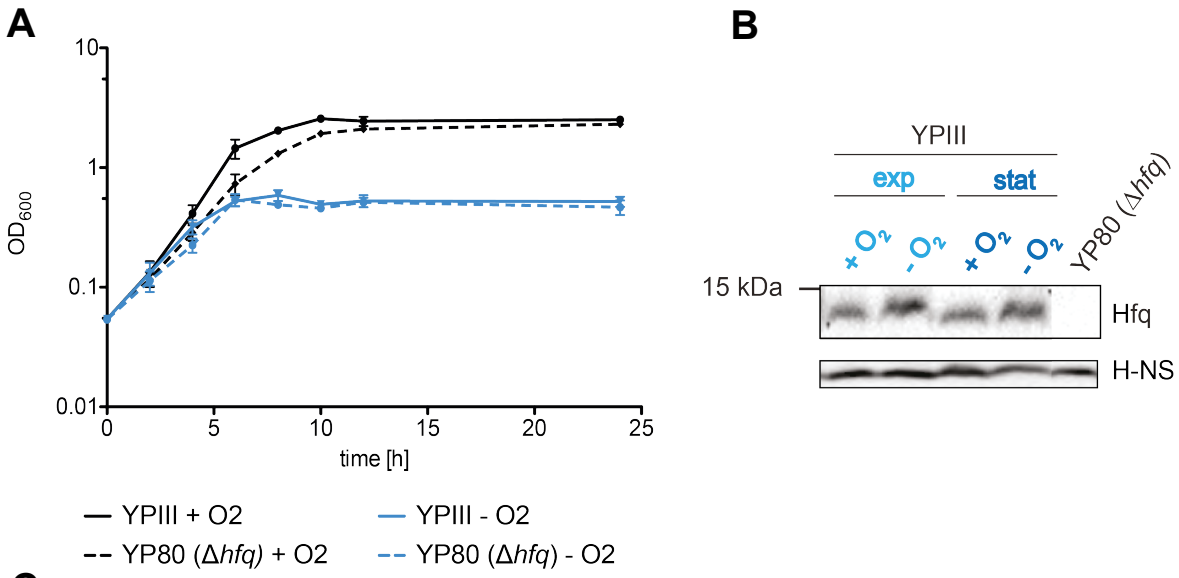
Oxygen limitation

To monitor the impact of Hfq in oxygen limiting conditions, LB medium was supplemented with 10 mg/l glucose and the bacteria were incubated in the presence or absence of O_2. Fresh medium was inoculated to a start OD_{600} of 0.05 and the growth was monitored for 24 h (Figure 48).

Limitation of oxygen slowed down the wild type growth ca. 2 fold, which was not reduced further in the *Δhfq* mutant strain.

The western blot analysis showed that Hfq protein levels were not significantly affected by oxygen limitation (Figure 48 B). Additionally, no growth phase-dependent expression was detectable. This indicates, that the addition of glucose might alter the Hfq protein levels. The LB medium used in this experiments was supplemented with 10 mg/l glucose, while previous experiments were carried out in LB medium, which was not supplemented with glucose (Figure 42).

This indicates, that Hfq is not involved in the response to limiting oxygen conditions. Additionally, the western blot analysis showed, that the expression of Hfq might be regulated by the availability of glucose.



C

	Growth rate [h^{-1}]	Doubling time [h]		Growth rate [h^{-1}]	Doubling time [h]
YPIII			**- O_2**		
LB	0.198	1.53	YPIII	0.198	1.53
LB - O_2	0.108	2.8	YP80 *(Δhfq)*	0.106	2.85

Figure 48: Influence of oxygen limitation on Hfq expression and the growth behavior of YPIII and its *Δhfq* mutant strain. LB medium supplemented with 10 mg/l glucose and 0.2 mM Hepes was inoculated with the respective strain to a start OD_{600} of 0.05 and the growth in the presence and absence of O_2 was monitored for 24 h. Growth was monitored at 25°C for three independent cultures of each strain. The error bars indicate the calculated standard deviation at reach time point. The growth rate was calculated in exponential growth and compared between the different strains. (A) Growth curve of the YPIII and the YP80 strain. (B) Hfq protein levels after growth of YPIII under normal and oxygen limiting conditions. Samples were taken in the exponential growth phase. (C) Growth rates and doubling time of all strains.

Oxidative stress

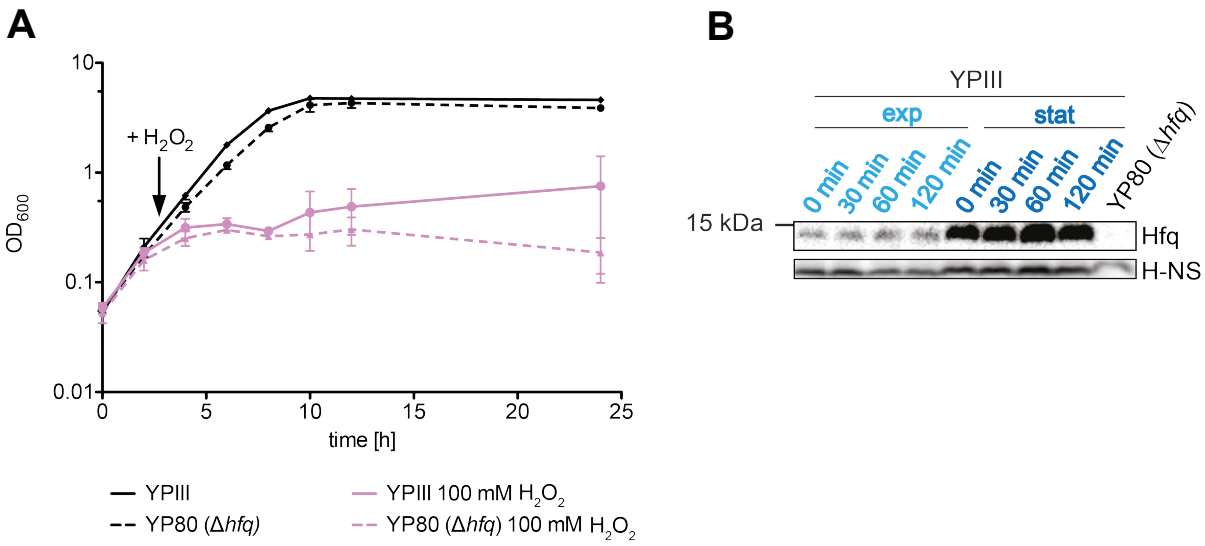
Previously, it was reported that the Δ*hfq* mutant in the *Y. pseudotuberculosis* clinical isolate IP32953 shows reduced intracellular survival in macrophages due to reduced survival after H_2O_2 stress (Schiano *et al.*, 2010).

To test whether the *Y. pseudotuberculosis* YPIII strain behaves similar the impact of oxidative stress on Hfq was also monitored. Oxidative stress was simulated by the addition of 100 mM H_2O_2, 1 mM diamide, or 50 µM paraquat.

To induce oxidative stress by H_2O_2 fresh LB medium was inoculated to a start OD_{600} of 0.05 and 3 h later 100 mM H_2O_2 was added. Growth was monitored for 24 h.

The addition of H_2O_2 led to approx. 7 fold slower growth of the wild type. The *Δhfq* mutant strain showed no significant different growth than the wild type (Figure 49). Both wild type and *Δhfq* mutant reached a 10 fold lower OD_{600} after 24 h.

To determine the impact of H_2O_2 stress on Hfq protein levels western blot analysis was carried out. 3 h post inoculation 100 mM H_2O_2 was added to analyze the influence of oxidative stress in the exponential growth phase. Additionally, 100 mM H_2O_2 was added to over night cultures to determine the impact in the stationary growth phase. Samples were taken at time point 0 and 30 min, 60 min, and 120 min post induction. After treatment the Hfq protein levels were similar to the untreated control (time point 0; Figure 49 B).



	Growth rate [h^{-1}]	Doubling time [h]		Growth rate [h^{-1}]	Doubling time [h]
YPIII			**Addition of 100 mM H_2O_2**		
LB	0.206	1.46	YPIII	0.033	9.88
LB H_2O_2	0.033	9.88	YP80 *(Δhfq)*	0.037	8.8

Figure 49: Influence of oxidative stress induced by H_2O_2 on growth of YPIII and YP80 (*Δhfq*) and the Hfq protein levels. LB medium was inoculated with the respective strain to a start OD_{600} of 0.05 and the growth was monitored for 24 h. Growth was monitored at 25°C for three independent cultures of each strain. The error bars indicate the calculated standard deviation at reach time point. The growth rate was calculated in exponential growth and compared between the different strains. (A) Growth curve of *Y. pseudotuberculosis* YPIII and YP80 (*Δhfq*). 3 h post inoculation 100 mM H_2O_2 was added. (B) Western blot against Hfq and H-NS after the addition of H_2O_2. Cultures were grown at 25°C for 3 h or 14-16 h, respectively, and 100 mM H_2O_2 was added. Samples were at the indicated time points. (C) Growth rates and doubling time of all strains.

Diamide and paraquat are chemical substances that produce reactive oxygen species. Diamide belongs to the class of reactive electrophilic species and influences the thiol redox balance in bacteria (Pöther *et al.*, 2009). In plants, paraquat increases the production of reactive oxygen species. Further, this compound inhibits the regeneration of reducing equivalents (Ramiro Lascano, 2012). These substances were used to induce oxidative stress in a long-term manner since H_2O_2 introduces only short-term stress (few hours). The reactive substances were added to the culture at the beginning of growth. Treatment of the wild type culture with 50 µM paraquat had significant influence on the growth rate. The addition of

the substance led to a 2 fold slower growth. The Δ*hfq* strain showed no difference in growth compared to the wild type grown under the same stress condition. 12 h and 24 h post inoculation/induction the wild type seems to start outgrowth (Figure 49 A).

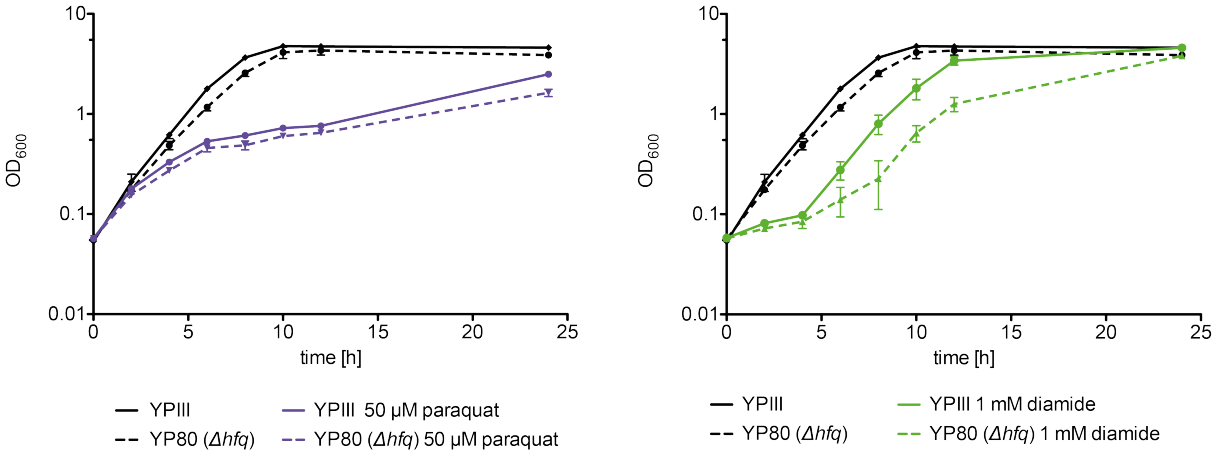
The addition of 1 mM diamide did not affect the growth rate of the wild type but the lag phase was extended to approx. 4 h vs. 1 h under non-stress conditions. Similar to the wild type the lag phase of the Δ*hfq* strain was extended to about 4 h after start of the cultivation. In contrast to the wild type the growth rate of the Δ*hfq* mutant strain was influenced. The doubling time of the Δ*hfq* strain was about 3 fold slower than that of the wild type (Figure 49 A).

Additionally, Hfq protein levels were affected by the addition of paraquat and diamide. In the stationary growth phase lower Hfq protein levels were detected by western blotting, indicating that *hfq* expression is affected in response to oxidative stress (Figure 50 B).

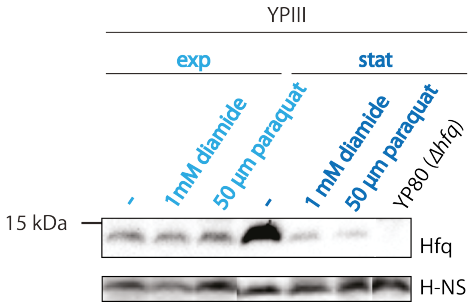
Taken together, these data indicate, that 1. Hfq is involved in oxidative stress response of *Y. pseudotuberculosis* YPIII (reduced growth) and 2. the *hfq* expression is affected by oxidative stress. Schiano *et al.*, 2010 reported, that *Y. pseudotuberculosis* IP32953 does not survive treatment with 100 mM H_2O_2, which most probably is also the case for the YPIII strain. Additionally, the experiments reported here indicate, that treatment with 1 mM diamide efficiently induces oxidative stress in *Y. pseudotuberculosis* without killing the bacteria.

However, Hfq is not involved in the response to NaCl stress, pH stress or in oxygen limiting conditions.

A



B



C

	Growth rate [h^{-1}]	Doubling time [h]		Growth rate [h^{-1}]	Doubling time [h]
YPIII			**1 mM diamide**		
			YPIII	0.163	1.85
LB	0.206	1.46	YP80 *(Δhfq)*	0.075	5.22
LB diamide	0.163	1.85			
LB paraquat	0.088	3.41	**50 µM paraquat**		
			YPIII	0.088	3.41

Figure 50: Influence of oxidative stress induced by (A) 50 µM paraquat or (B) 1 mM diamide on growth of both YPIII and YP80 and Hfq protein levels. LB medium supplemented with 1 mM diamide or 50 µM paraquat was inoculated with the respective strain to a start OD_{600} of 0.05 and the growth in the presence and absence of O_2 was monitored for 24 h. Growth was monitored at 25°C for three independent cultures of each strain. The error bars indicate the calculated standard deviation at reach time point. The growth rate was calculated in exponential growth and compared between the different strains. (A) Growth curve of the YPIII and the YP80 strain. (B) Hfq protein levels after growth of YPIII after the addition of diamide or paraquat. Samples were taken in the exponential growth phase. (C) Growth rates and doubling time of all strains.

4 Discussion

4.1 Identification of novel sRNAs in *Y. pseudotuberculosis* YPIII

In recent years is became evident, that sRNAs may act as global modulators and regulators of bacterial gene expression. An increasing amount of publications focused on the identification of regulatory sRNAs on a global level. Especially in pathogens, more and more sRNAs were identified in the last years, e.g. in *Helicobacter pylori*, *Clostridium difficile*, and *Pseudomonas aeroginosa* (Sharma *et al.*, 2010; Ferrara *et al.*, 2012; Soutourina *et al.*, 2013). This study aimed for the identification of novel sRNAs in the human pathogen *Y. pseudotuberculosis* YPIII. *Y. pseudotuberculosis* is a food-borne pathogen that is taken up orally and causes gut-associated diseases such as diarrhea. Two different approaches were used for sRNA identification. First, sRNAs were identified by 454 pyrosequencing with total RNA that was size fractionated. This enrichment allowed the identification of weakly expressed sRNAs, but the detection of the *Y. pseudotuberculosis* transcriptome was not possible. A second approach carried out later identified sRNAs by Illumina sequencing and in addition, the whole transcriptome of *Y. pseudotuberculosis* YPIII was analyzed.

For 454 sequencing total RNA was isolated from bacteria grown at 25°C to the stationary growth phase and at 37°C in exponential growth. These conditions were chosen, because they simulate infection conditions. A *Y. pseudotuberculosis* infection proceeds in two phases: during the initial infection the bacteria penetrate the epithelial layer of the small intestine and in the ongoing infection phase *Y. pseudotuberculosis* colonizes deeper organs such as liver, kidney, and spleen. The initial infection phase is simulated *in vitro* by growth at 25°C to stationary growth, which induces expression of characteristic virulence genes of the initial infection phase such as *invA* and *rovA* (Nagel *et al.*, 2001; Nagel *et al.*, 2003). In contrast, the ongoing infection phase is simulated by growth at 37°C to the exponential growth phase leading to the induction of the virulence plasmid-associated genes (Böhme *et al.*, 2012). Especially sRNAs that are expressed at 37°C in the exponential growth phase may be virulence-associated. Further, total RNA of an *hfq* deficient strain grown at 25°C to stationary growth was isolated and analyzed by 454 sequencing, since Hfq is an essential chaperone

helping sRNAs to perform their function. One would expect Hfq dependent sRNAs to be present in only one or the other strain.

The identification by Illumina sequencing was additionally performed after growth at 25°C to the exponential growth phase and at 37°C after stationary growth to broaden the potential of sRNA identification. Further, the influence of Crp on sRNAs was analyzed. In *Y. pseudotuberculosis* Crp is an essential virulence regulator controlling the expression of host-adapted metabolism associated genes (Heroven *et al.*, 2012). Therefore, this study also aimed to identify the whole Crp regulon including Crp-dependent sRNAs

With the first bioinformatic attempt analyzing the 454 sequencing data 320 sRNAs were detected out of which 20 were encoded on the virulence plasmid pYV. The bioinformatic settings used here defined an sRNA to have a size of 50-500 nts with a permanent coverage of 5 reads. The validation of these results by northern blot analysis failed for most selected candidates. Several explanations for these difficulties are possible. First, the detected sRNAs were false positive or below the detection threshold of northern blotting. Second, the sequencing depth was not deep enough to use these low stringent criteria for bioinformatic analysis. Indeed, the Illumina sequencing approach revealed that some of the RNAs were classified as 5' or 3' UTRs of the surrounding genes. For example, the 454 sequencing indicated an sRNA to be located on the negative strand between position 145659 and 145713 (YpseC0009, Figure 51). However, the Illumina sequencing including its bioinformatic analysis indicated that this transcript was not an sRNA but is the transcriptional start site of the following gene. The reads covering the 5' region of the transcript were highly abundant but the following part of the transcript was not. A sequencing depth that does not cover this low abundant downstream region of the transcripts in combination with too low stringency in the bioinformatic search criteria may lead to false positive identification of sRNAs. Therefore, the bioinformatic criteria were changed and an sRNA was defined to have a seed region with a coverage of ≥ 10 reads. To define the size of the sRNA this region was then extended to both sites until a coverage below 5 reads was reached. These criteria were also used previously (Schluter *et al.*, 2010).

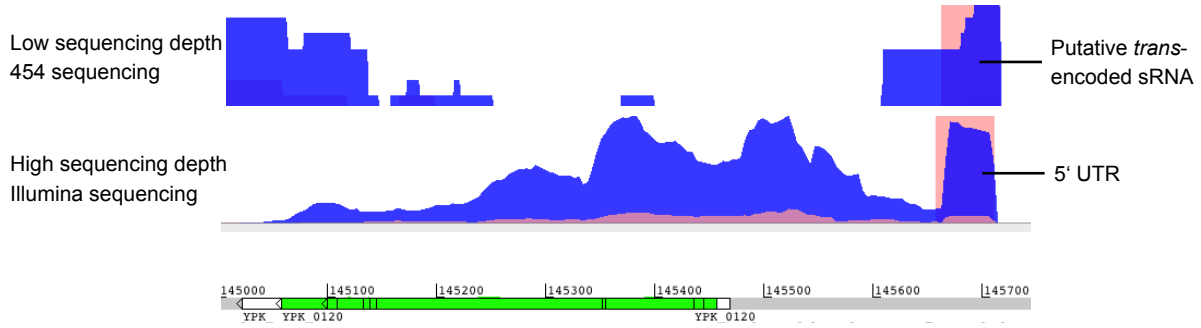


Figure 51: Screenshot of the Artemis genome browser illustrating the genomic region around the putative sRNA YpseC0009. A low sequencing depth (454 sequencing) identifies this region as an sRNA (upper panel). High sequencing depth (Illumina sequencing) identified this region as a 5' UTR (lower panel).

This reduced the number of sRNAs to 170 out of which five were encoded on the virulence plasmid pYV. 52 of those sRNAs were classified as *trans*-encoded sRNAs, 26 as *cis*-encoded antisense transcripts and 91 as mRNA leader structures. 39 previously identified sRNAs were no longer defined as such and 50 % of those were classified as TSS by Illumina sequencing. The remaining 50 % might either be *trans*-encoded sRNAs or the identification by Illumina sequencing as TSS failed due to insignificance. Further, the identification of *cis*-encoded sense sRNAs was renounced since these sRNAs might not be independent transcripts but rather processed transcripts of ORFs.

By Illumina sequencing 163 sRNAs classifying in *trans*- and *cis*-encoded antisense sRNAs were identified (83 and 80 sRNAs, respectively). Conspicuously, 18 of the antisense-encoded sRNAs were located on the virulence plasmid pYV, which is ¼ of all detected antisense sRNAs. However, detection of these sRNAs by northern blotting was difficult and only one candidate could be validated. Most probably this might be due to very low abundance of these sRNAs, which is indicated by low read counts in the Illumina sequencing.

Even though the same growth conditions were chosen, only 40 % of all identified sRNAs were detected by 454 and Illumina sequencing. In *Sinorhizobium meliloti* more than 1,000 sRNAs were identified. In their study the authors used Illumina sequencing, 454 sequencing and a microarray approach to detect as many sRNAs as possible. They were able to show that each method detected a different subset of sRNAs and only a minor overlap was present (Schluter *et al.*, 2010).

A first approach dealing with the bioinformatic identification of novel sRNAs in *Yersinia* predicted the existence of 1,478 putative sRNAs in *Y. pestis*. This is a very high number and indeed, more than 500 and 300 sRNAs, respectively, were detected in *Vibrio cholera* and *E. coli* (Liu *et al.*, 2009; Shinhara *et al.*, 2011). In the datasets reported here only a small number of sRNAs was detected, even though the bioinformatic prediction indicated much more sRNAs. One reason for this might be that additional sRNAs may only be expressed under other conditions, e.g. other environmental growth conditions, host cell contact, or during an infection. Indeed, preliminary data indicate that some sRNAs are only expressed during an infection but not in the tested *in vitro* conditions (Nuss, unpublished).

In the course of this work three studies were published dealing with the identification of novel sRNAs in the *Y. pseudotuberculosis* isolate IP32953 and two different *Y. pestis* strains. Yan *et al*., 2013, identified sRNAs in *Y. pestis* biovar microtus. By Illumina sequencing they identified 62 *trans*-encoded sRNAs and 16 antisense-encoded sRNAs. Only 13 already described sRNAs overlapped between their study and the 454 sequencing reported here. 16 already described sRNAs, one novel *trans*-encoded sRNA and one novel antisense sRNA were detected by them and the Illumina sequencing approach described in this study. Koo *et al*., 2011, and Beauregard *et al*., 2013, reported sRNAs in *Y. pseudotuberculosis* IP32953 and *Y. pestis* KIM6+. Both studies used Illumina sequencing and identified only *trans*-encoded sRNAs. Comparing these published sRNAs with the sRNAs identified by 454 pyrosequencing reported here showed that only 50 % of the sRNAs detected by 454 sequencing were also detected by Koo *et al*., 2011 and Beauregard *et al*., 2013. Similar, 50 % of the sRNAs detected by Illumina sequencing were present in these published datasets.

The question how this small overlap might be explained may be answered by strain specific (YPIII vs. IP32953) or medium specific sRNA expression (LB medium vs. BHI medium) or by different experimental setups. To address whether medium- or strain-specific sRNA expression might explain the small overlap the *Y. pseudotuberculosis* isolates YPIII and IP32953 were grown in LB and BHI medium and five sRNAs solely identified by Koo *et al*., 2011, were selected for northern blot detection. Only two of theses candidates were expressed in the YPIII background (Ysr10, Ysr12) out of which one could only be detected after growth in BHI medium (Ysr10). Detection in the IP32953 background was possible for all five candidates out of which three were only detectable after growth in BHI medium but not in LB medium (Ysr10, Ysr17, Ysr19). One sRNA was only detectable in strain IP32953 but

not in YPIII (Ysr18). These data indicate a strain- as well as medium-dependent expression of sRNAs. Medium-dependent expression of sRNAs was described previously. In *Streptomyces coelicolor* the sRNA scr1906 was only expressed in rich medium, while the sRNA scr3261 was only detectable after growth in minimal medium (Swiercz *et al.*, 2008).

When Beauregard *et al.,* 2013, compared their set of identified sRNAs to the sRNAs identified by Koo *et al.*, 2011, only half of the sRNAs were present in both studies. In addition, to the above mentioned explanations three further explanations were suggested by Beauregard *et al*., 2013. In addition to strain- and medium-dependent expression it might be possible that the detection of an sRNA was not possible due to the differences in bioinformatic analysis. To remove 5' and 3' UTRs Koo *et al.*, 2011, defined an sRNA to show an at least three-fold expression difference to the surrounding ORFs. Thereby, several sRNAs might be lost. Additionally, Koo *et al.*, 2011, carried out northern blotting for 49 sRNAs and the detection of 20 of these candidates failed. The expression of these sRNAs might either be below the detection limit of northern blotting or these sRNAs are false positive candidates. Another reason may be method-dependent detection limits. One could speculate that all detected sRNAs are present in *Y. pseudotuberculosis* and only a small pool was detected in one or the other study. This is supported by the relatively low overlap of sRNAs detected by 454 pyrosequencing and Illumina sequencing reported here.

Out of the 169 sRNAs identified by 454 sequencing about 50 % of the *trans*-encoded sRNAs (23 out of 52) and approx. 30 % of the *cis*-encoded antisense sRNAs (9 out of 28) were validated by northern blotting. The expression pattern of 11 sRNAs predicted by 454 pyrosequencing did not coincide with the expression pattern detected by northern blot analysis. For pyrosequencing total RNA was isolated by a normal column-based method in combination with an enrichment method for small sized fragments to detect as many sRNAs as possible. This enrichment was not carried out when RNA was isolated for northern blotting and may therefore explain the expression differences.

In total, the temperature- and growth-phase dependent expression of 30 sRNAs identified by Illumina sequencing was experimentally compared to the results of the global transcription profile (Table 10). Out of these the growth phase- and temperature-dependency was confirmed for 16 and 20 candidates, respectively (including those where up or downregulation was reported as well as those were no regulation was indicated). In four cases neither growth phase nor temperature profile matched the RNA-Seq. If no change in

gene expression was indicated by Illumina sequencing this might be due to insignificancy. The fold change of all three independently sequenced samples was determined and an overall fold change was calculated. The p-value was calculated indicating the variation between these three samples. If a p-value above 0.05 was present, the regulation was considered to be insignificant. Additionally, a coverage above 30 normalized reads needed to be present in at least one condition. In all cases only one of these requirements was not fulfilled but the tendency in the Illumina sequencing was consistent with the expression pattern detected by northern blotting. This indicates, that even less stringent bioinformatic criteria allow predicting the correct sRNA expression.

Further, contradictory expression patterns might be explained by different purification methods. For Illumina sequencing total RNA was isolated by the hot phenol method to reduce column-based biasing of the analysis. For northern blotting a column-based RNA isolation method needed to be used to yield high amounts of total RNA, which might bias the amount of purified RNA. Subsequent handling differences, e.g. centrifugation time, might lead to different RNA degradation and thereby to different expression patterns.

The expression profile of sRNAs that are well characterized in *E. coli* and *Salmonella* was analyzed in the course of this study. It was reported that nearly all of theses sRNAs show a upregulation in stationary growth, namely SraH, MicM, RybB, the processed form of GlmY, CyaR, and RyhB (Argaman *et al.*, 2001; Wassarman *et al.*, 2001; Vogel *et al.*, 2003; Papenfort *et al.*, 2006; Kalamorz *et al.*, 2007; Papenfort *et al.*, 2008; Papenfort *et al.*, 2009). By northern blotting this upregulation was also detectable in *Y. pseudotuberculosis*. This indicates that these sRNAs are involved in regulatory mechanisms that are widely conserved and are responsible for cell viability. In fact, SraH is involved in the uptake of serine and the response to oxidative stress while sRNAs like MicM and RybB regulate the expression of outer membrane proteins to maintain the membrane integrity (Papenfort *et al.*, 2006; Papenfort *et al.*, 2009). GlmY and GlmZ are important for the cell wall synthesis to ensure the availability of its core components (Kalamorz *et al.*, 2007; Reichenbach *et al.*, 2008). Furthermore, eight of the twelve newly identified sRNAs were also more abundant in the stationary growth phase. Sequencing of the transcriptome showed that stationary grown bacteria have a higher coverage of intergenic regions than exponentially grown bacteria. This indicates that the production of sRNAs is generally induced in the stationary growth

phase. The fact that not only the expression of many sRNAs but also the Hfq protein levels were strongly induced in the stationary growth phase supports this (Figure 41).

In contrast to the majority of sRNAs GlmZ, GcvB, and Spot42 sRNA levels were reported to be upregulated in the exponential growth phase (Kalamorz *et al.*, 2007; Sharma *et al.*, 2007; Hansen *et al.*, 2012). This finding could be proven for all three sRNAs when comparing only the amount during growth at one temperature.

Only the expression of FnrS, OmrA, and RyeB did not coincide with data published previously for *E. coli* and *Salmonella*. FnrS was reported to be only detectable under oxygen limiting conditions but the detection in *Y. pseudotuberculosis* was possible in the presence of oxygen (Boysen *et al.*, 2010). In *E. coli* OmrA and RyeB were reported to be upregulated in the stationary growth phase but in *Y. pseudotuberculosis* both sRNAs were more abundant in the exponential growth phase (Argaman *et al.*, 2001; Fröhlich *et al.*, 2012). This difference in the expression pattern might be explained by its expression control. In *Salmonella* RyeB is strongly dependent on the stationary growth phase sigma factor σ^S and it could be possible, that the regulation of *ryeB* is different in *Y. pseudotuberculosis.* Moreover, RyeB detected in *Salmonella* had a different size than in *Y. pseudotuberculosis* (Fröhlich *et al.*, 2012).

Eleven novel *trans*-encoded sRNAs and seven *cis*- encoded antisense sRNAs detected by 454 sequencing showed a multiple band pattern on the northern blot. The bands indicating a longer sized transcript indicate that the sRNAs might be transcribed as primary transcripts and are subsequently processed. This mechanism is quite well studied for the sRNAs GlmY and GlmZ (Kalamorz *et al.*, 2007; Reichenbach *et al.*, 2008). In nearly all cases 454 sequencing detected the small or medium sized transcripts but not the longer transcript, which might be a result of the enrichment for smaller sized fragments. The example of the sRNA YpseC0075 underlines this hypothesis. The 454 sequencing predicted a size of 55 nts, while the Illumina sequencing predicted a size of 254 nts. Further, these differences might be caused by the presence of different promoters or alternative terminator sequences. Similar results were detected in other organisms (Schluter *et al.*, 2010).

50 % of all sRNAs detected by 454 sequencing showed an Hfq dependency in *Y. pseudotuberculosis* YPIII. This was validated experimentally, since 28 of the 47 sRNAs that were confirmed by northern blotting showed an Hfq-dependency. However Koo *et al.*, 2011 reported, that no Hfq dependency is present in *Y. pseudotuberculosis* IP32953. In *Y. pestis* the same sRNAs were Hfq dependent. Therefore, the authors state, that differential

posttranscriptional regulation might explain the diverge disease outcome of *Y. pseudotuberculosis* and *Y. pestis* (Koo *et al.*, 2011). The data presented here indicate, that strains within one species differentially express sRNAs in a strain-dependent, medium-dependent, and Hfq-dependent manner. This indicates, that not only posttranscriptional regulation distinguishes *Y. pseudotuberculosis* and *Y. pestis* but even different isolates within one species.

In a Δ*hfq* mutant strain, the transcriptional activity of the of the *fnrS, ryhB, spot42,* YpseC0083, and YpseC0125 promoter region was higher in at least one tested condition. The 454 pyrosequencing indicated lower FnrS, RyhB, and YpseC0125 sRNA levels in the absence of Hfq, which could be confirmed by northern blotting. It is likely that the bacteria react on this lower sRNA levels by an increased transcription rate.

Spot42 is an sRNA that regulates the expression of the *gal* operon in *E. coli*. It was reported that Hfq is required for the stabilization of the sRNA (Moller, Franch, Hojrup, *et al.*, 2002). Both northern blot analysis as well as the promoter-*lacZ* gene fusions showed no Hfq dependency in the YPIII strain indicating a different regulation in *Y. pseudotuberculosis*. Further, Beisel and Storz, 2011, reported that Crp represses Spot42 and this negative regulation was also detected for *Y. pseudotuberculosis* YPIII by Illumina sequencing. One explanation for the elevated Spot42 levels in a Δ*hfq* deletion strain would be a regulatory effect of Hfq on Crp. Indeed, in a Δ*hfq* strain lower Crp levels were detectable (Heroven, unpublished), which then results in an activation of Spot42 production. Beauregard *et al*., 2013, also recognized, that in some cases the influence of *hfq* on sRNA expression is specific to one temperature. Therefore, they proposed that complex interactions between temperature and *hfq* dependence might exist.

In addition, generally low β-galactosidase activity indicating a low transcription rate was detected (especially *micM* and YpseC0201), even though clear bands were detectable by northern blotting. This indicates that the sRNAs might be very stable. Indeed, the half-life of MicM is approx. 25 min indicating a very stable sRNA. In *E. coli* MicM is necessary to downregulated a porin under normal growth condition in a complex manner. Upon the availability of the corresponding stimulus MicM is degraded and the mRNA of the porin is translated. Since the porin mRNA only needs to be translated regulation via MicM allows a faster response to the changing environmental conditions (Overgaard *et al.*, 2009).

Out of the 163 sRNAs identified by Illumina sequencing nine were only detected after the sequencing of a Δ*crp* deletion strain. Surprisingly, 91 sRNAs showed a Crp-dependent expression. This indicated, that the global regulator Crp not only regulated gene expression but also the expression of many sRNAs. In *P. aeroginosa* the global regulator AmpR was also shown to regulate the expression of several sRNA. AmpR is involved in antibiotic resistance and regulates iron uptake and oxidative stress. AmpR influences the expression of the sRNA rgP32, which controls the heat shock response (Balasubramanian *et al.*, 2013).

Northern blotting validated Crp-dependency of twelve candidates. The expression pattern of ten candidates was consistent with the data indicated by Illumina sequencing, while one sRNA (YPK_transRNA_71) showed a different expression profile. MicM and GlmY showed only a very low dependency on Crp. Surprisingly, in all cases higher sRNA levels were detectable in the *crp* deletion strain grown at 25°C compared to 37°C. This might indicate, that the deletion of *crp* leads to a completely different composition of the total RNA.

To address, weather regulation of sRNA expression by Crp is direct, binding site predictions were carried out. 200 nts upstream and 100 nts downstream of the predicted TSS were screened for the Crp consensus motif ($TGTGAN_6TCACA$) and binding sites were predicted for 24 sRNAs.

Crp binding to the upstream region of ten candidates was analyzed by EMSA. The highest binding affinity was detected to the upstream region of *crp2*. This region carries a perfect binding site for Crp, which explains this high affinity. Similar, the promoter regions of YPK_transRNA_38 and YPK_transRNA_71 were bound with a much higher affinity than the *cyaR* and *omrA* upstream region. Both *cyaR* and *omrA* carry one Crp binding site with two mismatches. YPK_transRNA_38 carries one perfect binding site, while the upstream region of YPK_transRNA_71 carries four Crp binding sites, one with a perfect match, one with one mismatch, and two with two mismatches to the consensus sequence. These differences in the Crp binding sites may explain the different binding affinities of the protein. In *E. coli* the promoter region of the *fumA*, *fumC,* and *rmf* genes were bound by the Crp-cAMP complex. *fumA* carries one Crp binding site with a total of three mismatches, while *fumC* carries two Crp binding sites with two and three mismatches, respectively (Chen *et al.*, 2012; Shimada *et al.*, 2013). In *Y. pestis* the *cyaA* promoter region carries one perfect Crp binding site and the expression is regulated by direct Crp binding (Qu *et al.*, 2013).

A recent study also identified novel Crp-dependent sRNAs. In contrast to the study reported here, they identified sRNAs only after growth in rich or minimal medium or in infected organs but a Δ*crp* deletion strain was not sequenced. Subsequently, 100 nts of the upstream region of these sRNAs were analyzed with respect to the presence of the Crp consensus motif. Thereby, ten sRNAs were identified to carry a Crp binding site. Northern blotting experiments showed, that four of those were indeed Crp dependent (Yan *et al.*, 2013).

Previous studies have already reported that Crp regulates CyaR (Papenfort *et al.*, 2008). Both northern blot and EMSA confirmed this for *Y. pseudotuberculosis*. In *Y. pseudotuberculosis* and *E. coli* the cAMP/Crp complex bound the *cyaR* promoter region at similar amounts of protein and DNA.

Five additional candidates did not show a specific or very weak binding of cAMP/Crp to their upstream region, while four of these candidates showed a Crp-dependent sRNA expression (YPK_asRNA_30, YPK_transRNA_73, GcvB, MicA). This indicates that the regulation via Crp is indirect. Similar results were reported previously for the sRNAs CsrB and CsrC (Heroven *et al.*, 2012).

Small regulatory RNAs may also influence the virulence of pathogens. In *S. pneumonia* single deletion of eight different sRNAs resulted in lower mortality of infected mice (Mann *et al.*, 2012). The sRNA FtrC of *Franciesella tularensis*, the causative agent of tularemia did also influence the virulence of this pathogen, when the sRNA was overexpressed (Postic *et al.*, 2012). In *Yersinia* a deletion of the RNA thermometer in front of *lcrF* led to attenuated virulence (Böhme *et al.*, 2012), while the deletion of the RyhB1 and RyhB2 sRNAs did not influence the virulence (Deng *et al.*, 2012). The *Y. pseudotuberculosis* sRNAs Ysr29 and Ysr35 influenced the mortality of infected mice (Koo *et al.*, 2011). Since the impact of only a few sRNA on *Yersinia* virulence is studied, this study aimed to elucidate the impact of selected sRNA candidates on the virulence of *Y. pseudotuberculosis*.

In *E. coli* CyaR and MicA were reported to negatively regulated *ompX, ompA,* and *phoP* (Udekwu *et al.*, 2005; De Lay and Gottesman, 2009; Coornaert *et al.*, 2010). All proteins were shown to be essential for *Yersinia* virulence (Fisher *et al.*, 2007; Kolodziejek *et al.*, 2010; Bartra *et al.*, 2012). Additionally, both sRNAs were highly expressed in *Y. pestis* after mouse infection (Yan *et al.*, 2013). Therefore, these sRNAs were chosen to analyze their impact on the virulence of *Y. pseudotuberculosis* IP32953 using the mouse model. However, the deletion of neither *cyaR* nor *micA* altered the virulence of *Y. pseudotuberculosis* IP32953. A

In Y. pestis a deletion of cyaR did also not affect the virulence (Yan *et al.*, 2013)Similar results were detected for the sRNA FtrC in *F. tularensis*. Deletion of this sRNA did not affect the replication in macrophages, but an overexpression inhibited the intracellular replication. Further, mouse experiments showed that bacteria overexpressing FtrC colonized spleen and liver less efficiently (Postic *et al.*, 2012). It might be possible, that overexpression of *cyaR* and *micA* in *Y. pseudotuberculosis* would also lead to a virulence-associated phenotype. Since both sRNAs inhibit the production of virulence factors, a deletion would lead to higher amounts of OmpA, OmpX, and PhoP, while an overexpression would inhibit their production. Assuming that these factors are crucial for virulence and their expression is induced upon infection deletion of negative regulators would not be recognized. However, it might also be possible, that *micA* and *cyaR* do not influence the virulence of *Y. pseudotuberculosis*.

4.2 Transcriptomic profiling of *Y. pseudotuberculosis* YPIII

In this study the transcriptomic landscape of the human pathogen *Y. pseudotuberculosis* YPIII in response to temperature and growth phase was analyzed for the first time. Furthermore, the influence of the global regulator Crp was examined, since it is absolutely required for the virulence of *Y. pseudotuberculosis* (Heroven *et al.*, 2012). Using qRT-PCR the growth phase- and temperature-dependent gene expression was confirmed for 17 and 21 candidates, respectively. The transcriptome of the isogenic Δ*crp* strain was analyzed in the stationary growth phase at 25°C or 37°C.

Illumina sequencing has the advantage that the total RNA of a bacterial cell is sequenced and a quantitative analysis of these data is possible similar to microarrays. In comparison to microarrays, deep sequencing allows a much more sensitive detection of differentially regulated genes (Baginsky *et al.*, 2010). In total, 563 genes were detected to show a varying expression profile in the wild type and the Δ*crp* mutant at 25°C, while a microarray approach identified only 344 genes (Heroven *et al.*, 2012). 75 % of the genes identified by microarray were also found by Illumina sequencing. A study in *P. aeroginosa* compared microarrays to RNA-Seq. In their study only 50 % of the genes identified by microarray were also detected by Illumina sequencing. In total, a higher number of differentially regulated genes was detected by Illumina sequencing (Balasubramanian *et al.*, 2013).

The growth phase-dependent transcriptome

The transcriptome of *Y. pseudotuberculosis* YPIII grown at 25°C in exponential phase was compared to the transcriptome of bacteria grown in stationary phase. In the exponential growth phase, high amounts of nutrients are available, which enable the bacteria to grow fast and anabolize the available nutrient. In the stationary growth phase lower amounts of nutrients are available. This means, that the energy availability is lower and the bacteria are occupied with maintenance (Sest, 2012). Mainly genes involved in translation and amino acid and carbohydrate metabolism were influenced. These results stand in good agreement with the growth phase-dependent transcriptome of *Acinetobacter baumannii*, where many amino acid metabolism-associated genes, nucleotide transporters, and translation-associated genes were influenced by the growth phase (Jacobs *et al.*, 2012).

The major groups of upregulated genes in the stationary growth phase were amino acid and carbohydrate metabolism-associated genes indicating that the bacteria switch their set of metabolic genes to be able to survive in low nutrient conditions. *astABE* were upregulated during stationary growth, which are involved in the arginine succinyltransferase pathway. In this pathway ammonia is liberated which bacteria need to survive (Y Han *et al.*, 2004). *hisPGJ* encoding for a histidine transporter were upregulated allowing the bacteria to take up this amino acid (Motin *et al.*, 2004). In total, more than 40 amino acid and carbohydrate metabolism-associated transporters were upregulated in stationary growth. Genes coding for the uptake of dipeptides (*dppA-F*) and oligopeptides (*oppA-D*) were induced in the stationary growth phase, which were shown to be regulated in an RpoS dependent manner in *E. coli* (Dong and Schellhorn, 2009). Additionally, genes involved in the β-oxidation (*frdA-D*) were upregulated in the stationary phase allowing the production of acetyl coenzyme A (Motin *et al.*, 2004). This can then further be utilized in the glyoxylate cycle, which was also upregulated in the stationary growth phase (*aceAB, acnA*). The glyoxylate cycle is induced if carbon sources are limited which is the case in the stationary growth phase (Kim *et al.*, 2004). The urease subunits *ureABC* were also upregulated during nutrient starvation. This enzyme is necessary in acidic pH to catalyze the hydrolysis of urea to ammonia and CO_2. It is essential for *Yersinia* to survive in an acidic environment (De Koning-Ward and Robins-Browne, 1995). Additionally, *fruABK* were upregulated, which are involved in the utilization of fructose (Kornberg, 2001). However, the same amount of amino acid metabolism associated genes was downregulated in the stationary growth phase. In general,

lower transcriptional and translational activity can be assumed in the stationary growth phase, since less energy is available. Further, only few bacteria divide. This is indicated by a downregulation of translation-associated genes such as ribosomal proteins. In *E. coli* it was also shown, that the concentrations of ribosomes within a cell is proportional to the growth rate (Bugrysheva *et al.*, 2011).

Many virulence-associated genes were upregulated in the stationary growth phase. The primary invasion factor *invA* and its positive regulator were induced. Similar, the afimbrial adhesion operon *psaABC* and its positive activator *psaEF* were induced. These proteins were shown to be necessary for hemagglutination and binding to epithelial cells (Yang *et al.*, 1996). In *E. coli*, the transcriptome after deletion of the stationary phase σ-factor *rpoS* was analyzed (Patten *et al.*, 2004). Many genes, that were found to be up- or downregulated by *rpoS* were regulated in the same manner in the Illumina sequencing reported here. Only in a few cases contradictory results were found. One such example are the genes coding for the Suf machinery, which is responsible for the biosynthesis of Fe-S clusters under iron starvation conditions (Singh *et al.*, 2013).

The temperature-dependent transcriptome

Comparing the expression levels of exponentially grown bacteria at 25°C or 37°C showed that mostly translational, cell motility, and amino acid metabolism associated genes were downregulated. Another subset of amino acid metabolism associated genes as well as genes involved in energy conservation, carbohydrate metabolism and virulence were upregulated at 37°C. This strongly hints to the fact that the bacteria adapt their metabolism to host conditions. The nutrient availability during an infection is limited. To most efficiently use the available energy sources carbohydrate and amino acid metabolism is adapted to these conditions. Similar results were detected for *Y. pestis.* A temperature shift from 26°C to 37°C affected amino acid metabolism associated genes in both positive and negative manner. In *Y. pestis* the *ast* operon was upregulated at 37°C which helps the cells to liberate ammonium (Han *et al.*, 2004; Motin *et al.*, 2004). The data presented here also indicate this upregulation in *Y. pseudotuberculosis*. This suggests that both pathogens have a higher need of ammonia at 37°C. The production of virulence factors is a very energy consuming process. In *Y. pestis* genes coding for TCA cycle proteins were induced upon temperature shift. TCA cycle associated genes such as *fumA*, *gltA*, *acnAB*, and *sucABC* were also upregulated in

Y. pseudotuberculosis YPIII grown at 37°C. This indicates that both pathogens may enhance energy production by the TCA cycle in the mammalian tissue (Motin *et al.*, 2004). *E. coli* and *Salmonella* also rely on the TCA cycle during an infection. Induction of TCA cycle enzymes during urinary tract infection supports virulence of *E. coli*. Disruption of the TCA cycle resulted in reduced colonization of the bladder and the kidney (Alteri *et al.*, 2009). In *Salmonella* deletion of genes that encoded for enzymes of the TCA cycle resulted in an attenuated phenotype (Yimga *et al.*, 2006). Further, genes associated with fatty acid degradation were upregulated at 37°C (*fadJ, fadD*), which subsequently provide the TCA cycle with acetyl coenzyme A. At 25°C *fabA* and *fabF* were induced, which are necessary for fatty acid synthesis. This is consistent with data published for *Y. pestis*. In this pathogen fatty acid synthesis was also induced at 26°C (Motin *et al.*, 2004). Similar to *Y. pestis* (Motin *et al.*, 2004) *dadA, ansB*, and *putA* were upregulated at 37°C, which are necessary to generate α-keto acids that enter the TCA cycle.

In contrast to *Y. pestis* (Y Han *et al.*, 2004), genes coding for the growth on fumarate (*frdA-DF*) were upregulated at 37°C. These genes are necessary for the bacteria to be able to grow by anaerobic respiration with fumarate as electron acceptor. Therefore, the upregulation of this gene cluster might help *Y. pseudotuberculosis* to survive in the anaerobic condition of the intestine. The *atpB-EGHI* operon encoding for the ATP synthase was highly expressed at 25°C, which might explain the optimal growth temperature of the bacterium.

Not only the growth phase influenced the expression of the *hisMJQP* transporter, but also temperature. At 37°C the expression of these genes was induced allowing the bacteria to take up this amino acid (Motin *et al.*, 2004).

It was found, that the peptide chain elongation is faster at higher temperature, which might lead to incorrect folded proteins. This would require a heat shock response to counteract incorrect protein folding (Farewell and Neidhardt, 1998). Indeed, the major heat shock factors *groEL* and *groES* were induced at 37°C. At 25°C cold shock proteins such as *cspABC* were upregulated.

Additionally, translation-associated genes were downregulated at 37°C in *Y. pestis*, indicating that generally a bigger pool of proteins might be present at 26°C (Han *et al.*, 2004). In *Y. pseudotuberculosis* translation-associated genes were also downregulated at 37°C.

The downregulation of cell motility has advantages as well as drawbacks. It is generally believed, that *Y. pseudotuberculosis* needs flagella in the initial phase of an infection (25°C, stationary growth) and the expression is downregulated in the later stages of the infection (37°C, exponential growth). It could be shown for *Y. enterocolitica* that cell motility is necessary for the bacteria to efficiently reach the host cells (Young *et al.*, 2000). Therefore, a downregulation of FlhDC and subsequently the flagella proteins would lead to a disadvantage at host temperature. However, flagellin induces the production of proinflammatory signals in the mammalian host. Therefore, the downregulation of flagella in the human environments would be beneficial for *Y. pseudotuberculosis* (Ramos *et al.*, 2004). Simultaneously, the master regulators of cell motility FlhDC repress the expression of Yop protein (Bleves *et al.*, 2002). Downregulation of FlhDC at 37°C could therefore ensure, that the Yop proteins are produced upon host cell contact.

Nearly all structural components of the T3SS were upregulated at 37°C (YscC, YscJ, YscQ, YscRSTUV, YscKL. YopBD, LcrV). This ensures that the injectisome is build up at the bacterial cell to fight the immune system. The transcription of the translocated proteins YopM, YopH, YopP/J, and YpkA was also induced.

In *Mycobacterium tuberculosis* it was shown, that sulfur assimilation is necessary for virulence (Bhave *et al.*, 2007). *cysDHNI* were also upregulated at 37°C in *Y. pseudotuberculosis* indicating that this pathway might also be necessary for the bacteria during virulence.

In general, these data are consistent with studies performed in other γ-proteobacteria. Similar to the data presented here *L. monocytogenes* downregulates motility, amino acid metabolism associated genes and translation associated genes at 37°C (Garmyn *et al.*, 2012). Similar, temperature affected amino acid metabolism-associated genes in both positive and negative manner. Carbohydrate metabolism-associated genes as well as genes involved in the energy production were upregulated at 37°C in *P. aeruginosa* (Wu *et al.*, 2012). Cold shock and heat shock-associated genes as well as genes involved in fatty acid degradation were regulated in the same temperature dependent manner in *Moraxella catarrhalis* (Spaniol *et al.*, 2013).

Influence of Crp on gene expression

In addition, a Δ*crp* mutant was sequenced to identify the Crp regulon at 25°C and 37°C. Mainly genes involved in energy, carbohydrate, and amino acid metabolism were differentially regulated, which is in good agreement with previously published microarray data identifying the differential gene expression at 25°C in a Δ*crp* mutant (Heroven *et al.*, 2012). Additionally, many of the differentially regulated genes were also found to be differentially regulated in a Δ*crp* mutant in *E. coli* (Zheng *et al.*, 2004), while several genes carrying a putative Crp binding site in *M. tuberculosis* (Akhter *et al.*, 2008) were also found to be differentially regulated.

Heroven *et al*., 2012, showed that Crp induces oxidative phosphorylation mediated by the TCA cycle and the ability to utilize a verity of carbohydrates. This could also be detected by Illumina sequencing. TCA cycle-associated genes such as *fumA*, *rcs*, *mdh*, *sdhC*, and *frdABCD* were downregulated in a Δ*crp* mutant grown at both temperatures. Furthermore, cytochromes were repressed (*cyoAB*) at both temperatures. The downregulation of the TCA cycle also explained the downregulation of genes associated with fatty acid degradation in the Δ*crp* mutant after growth at 25°C or 37°C. Fatty acid degradation is used to feed acetyl coenzyme A into the TCA cycle (Motin *et al.*, 2004).

Genes involved in anaerobic respiration using fumarate as electron receptor were downregulated in a Δ*crp* mutant after growth at 25°C. This indicates, that Crp might be involved in the regulation of anaerobic respiration. In *Salmonella pepT* was reported to be positively regulated by Crp. This aminotripeptidas cleaved the N-terminal amino acid of tripeptides and is induced under anaerobic conditions (Lombardo *et al.*, 1997). The Illumina sequencing reported here indicated this peptidase to be Crp-dependent, since lower levels were detected in the Δ*crp* mutant strain supporting the hypothesis that Crp is involved in the regulation of anaerobic respiration. Additionally, genes involved in the assimilation of sulfur were upregulated in a Δ*crp* mutant at both temperatures. This might suggest, that Crp is necessary to control sulfur assimilation.

Consistent with the data published by Heroven *et al*., 2012, genes of the nucleotide transport and metabolism were upregulated after deletion of *crp* and growth at 25°C and 37°C, which were found to be involved in the increased utilization of nucleosides.

At 25°C genes involved in glycolysis were upregulated (*eno*, *glgAP*, *pckA*) in the absence of Crp. Further, genes encoding for components of the phosphotransferase systems, e.g. *manX*,

fruAKB, and *mglABC* showed a differential regulation at 25°C. In contrast, at 37°C glycogen degradation associated genes (*glgP*, *glgX*) were upregulated. The phosphotransferase-associated genes *ptsP*, *crr,* and *mglA*/B were also differentially regulated in the Δ*crp* mutant at 37°C.

Crp was reported to interconnect virulence and metabolism. As published previously (Heroven *et al.*, 2012), in the absence of Crp at 25°C the expression of the primary invasion factor *invA* and its transcription regulator *rovA* was downregulated after Illumina sequencing. In addition, *flhDC* and flagella assembly and motor proteins were downregulated in a Δ*crp* mutant grown at 25°C. Cell motility is essential for *Yersinia* to efficiently reach the host cells (Young *et al.*, 2000). Furthermore, T3SS proteins were downregulated at 25°C. This indicates that Crp might act as a positive regulator of Yop secretion, which was also shown in *Y. pestis* and *Y. enterocolitica* (Petersen and Young, 2002; Kim *et al.*, 2007). In addition, the Type VI secretion system 4 (T6SS4) was upregulated at 25°C in a *crp* deletion strain. In *Vibrio cholera* a T6SS was shown to be necessary for full virulence towards host cells. Further, in other γ-proteobacteria T6SSs are necessary to eliminate competitor bacteria (Gueguen *et al.*, 2013). This indicates, that Crp is necessary for the bacteria to prepare themselves for survival in the intestine.

As already mentioned, Yop secretion was reduced in *Y. enterocolitica* and *Y. pestis* Δ*crp* mutants at 37°C in Ca^{2+} depleted medium (Petersen and Young, 2002; Kim *et al.*, 2007; Heroven *et al.*, 2012). At 37°C the transcription of many injectisome coding genes such as *yscC*, *yscQ*, *yscRSTUV*, and *yscK* was upregulated in a Δ*crp* deficient strain but the expression of *yop* genes was not affected. These results might suggest that the reduced Yop secretion is not due to downregulation of the T3SS needle or a direct effect of Crp on Yop production. LcrV forms the tip of the needle and was downregulated in the Crp deficient strain. Previous studies have shown that LcrV is required for Yop production and secretion (Pettersson *et al.*, 1999). Therefore, one could speculate the downregulation in Yop secretion might be due to the absence of LcrV in a Δ*crp* strain rather than a direct effect on Yop production and the T3SS itself.

Further, the deep sequencing data indicated, that Crp regulates gene expression in a growth phase dependent manner. This is supported by the Crp expression profile. Similar to Hfq, Crp is strongly upregulated in the stationary growth phase and only small amounts are present in the exponential growth phase (Nuss, unpublished).

Global mapping of mRNA TSS

In many cases transcription of a gene starts upstream of the translational start site. These transcribed but not translated regions are called 5' UTR. They are also involved in gene regulation since they can form secondary structures, which enable them to function as RNA thermometers or riboswitches. RNA thermometers sense the temperature and may refold upon temperature shift, allowing or repressing translation. Riboswitches are able to bind small compounds, which may alter their structure. Thereby, transcription may be induced or repressed or the translation rate may be influenced (Naville and Gautheret, 2009).

In many cases deep sequencing samples were treated with Terminator Phosphate Dependent Exonuclease (TEX, e.g. Sharma *et al.*, 2010). This enzyme degrades all processed transcripts and allows the identification of primary transcripts and transcriptional start sites but it does not allow the quantitative analysis of gene expression. In the study reported here a different approach was used to identify TSS. In addition to TAP treated samples TAP untreated samples were sequenced.

The identification of TSS showed that the average size of the 5' UTR was 107 nts. 329 5' UTRs had a length between 20-40 nts. This is consistent with data published for *E. coli*, where an average TSS length of 112 nts was reported. Out of the 1441 putative TSS identified in *E. coli* 371 carried a 5' UTR of 20-40 nts (Mendoza-Vargas *et al.*, 2009). The average size of 5' UTR in *Salmonella* is 65 nts (Kröger *et al.*, 2012). A very low number of leaderless mRNAs was detected (15 in total), which is generally described for γ-proteobacteria (Zheng *et al.*, 2011). Leaderless mRNAs start either directly at the start codon or a few nts upstream. For translation initiation of these mRNAs it was proposed, that the ribosomes bind the translation initiation factor IF2, which helps to bind the initiation tRNA. The AUG is then recognized by the initiation tRNA (Moll *et al.*, 2002). A recent study in *E. coli* showed, that the endoribonuclease MazF specifically cleaves the 5' UTR of mRNAs to generate leaderless transcripts. In addition, MazF cleaves the 16S rRNA of the ribosome. This subdivision of ribosomes then specifically recognize the cleaved leaderless mRNAs (Vesper *et al.*, 2011).

The predicted TSS of ten candidates was verified by 5' RACE. Four candidates carried one TSS, which was confirmed. The remaining six candidates were predicted to have two TSS, which were confirmed for four candidates. One TSS of the remaining two candidates was confirmed, while the second TSS was not confirmed. An explanation might be the different

RNA isolation methods, which might lead to degradation of the 5' UTR (hot phenol vs. column-based method).

The approach performed here predicted the TSS of 25 genes to be located several nts downstream of the annotated translational start. A study identifying transcriptional start sites in *Salmonella* identified 93 out of 2695 TSS to be located downstream of the annotated position (Ramachandran *et al.*, 2012). In *E. coli* only a few TSS were reported to be located downstream of the annotated TSS with a majority being located more than 50 nts downstream (Cho *et al.*, 2009). This might be due to an incorrect annotation of these genes. The translational start sites of theses 29 genes were compared to the translational start sites of the *Y. pseudotuberculosis* wild type strain IP32953. Interestingly, in the IP32953 strain the annotated translation start of YPK_0122, YPK_0519, YPK_1275, YPK_1868, YPK_1252, YPK_2180, and YPK_2980 were differently annotated as in the YPIII strain. The annotation in the IP32952 strain started several nts downstream compared to the YPIII strain. This indicates, that the translational start site of at least these seven genes can be considered to be located downstream of the annotated translational start in the YPIII background. This is consistent with data published for *P. aeruginosa*. Here, global TSS identification after RNA-Seq allowed the reannotation of 46 genes (Wurtzel *et al.*, 2012).

4.3 Hfq and its role in *Y. pseudotuberculosis* YPIII

The RNA chaperone Hfq is important for many sRNAs to perform their function, since it enhances the RNA-RNA interaction between the sRNA and the mRNA (Wagner, 2013). Additionally, it was shown, that it is an important virulence factor for many bacteria. Deletion of *hfq* in *Y. pseudotuberculosis* and *Y. pestis* resulted in an attenuated virulence (J Geng *et al.*, 2009; Schiano *et al.*, 2010). In many other pathogens Hfq is also necessary for virulence, e.g. in *E. coli, P. aeruginosa, Salmonella, S. flexneri, Bordatella pertussis*, and *Haemophilus influenca* (Sharma and Payne, 2006; Sittka *et al.*, 2007; Hempel *et al.*, 2013; Meng *et al.*, 2013; Bibova *et al.*, 2013).

The expression of *hfq* was intensively studied in *E. coli* and *S. flexneri* (Figure 13). So far only negative regulators of *hfq* were identified. In *E. coli* the transcription of *hfq* is repressed by the Crp-cAMP complex by direct binding near promoter P3 (Lin *et al.*, 2011). The DksA protein binds further upstream in the promoter region and activates *hfq* transcription

(Sharma and Payne, 2006). Posttranscriptionally, the Hfq protein itself controls its expression. Binding to its mRNA leads to a translation inhibition (Vecerek *et al.*, 2005). Further, the CsrA protein inhibits translation of the *hfq* mRNA by binding to the SD sequence of the mRNA, which prevents ribosomes from binding (Baker *et al.*, 2007). The regulatory cascade controlling *hfq* expression in *Yersinia* is not yet known. Therefore, this study aimed to characterize the expression control of *hfq* in *Y. pseudotuberculosis* YPIII.

In this study it was shown that *hfq* expression is maximal in the stationary growth phase. This is consistent with high expression rates of sRNAs in the stationary growth phase. Since most sRNAs rely on Hfq it is necessary to increase its expression when many sRNAs are present. The influence of CsrA and Crp on *hfq* expression was also analyzed. Consistent with the data published by Heroven *et al.,* 2012, Crp had no effect on the Hfq protein levels. Further, deletion of *csrA* did not alter the expression of *hfq*. This indicates, that different regulatory mechanisms exist in different *Enterobacteriaceae*, which could also result in differential regulation of sRNA subsets. Indeed, the sRNAs FnrS, OmrA/B, and RyeB were differentially regulated in *Y. pseudotuberculosis* and *E. coli* or *Salmonella* (Argaman *et al.*, 2001; Boysen *et al.*, 2010; Fröhlich *et al.*, 2012).

Even though the regulation of *hfq* expression is not characterized in *Yersinia*, it was shown, that the protein is necessary during different stress conditions. In *Y. pestis* Hfq is involved in the resistance to heat and oxidative stress, nutrient limitation, and antibacterial peptide (J Geng *et al.*, 2009). In *Y. pseudotuberculosis* IP32953 deletion of *hfq* resulted in higher sensitivity to oxidative stress and higher motility at 26°C. Additionally, Hfq influences the secretion of Yop proteins (Schiano *et al.*, 2010). A major difference between the two pathogens is the influence of Hfq on growth. At 37°C a *Y. pestis* Δ*hfq* mutant showed a strong growth defect. However, the growth in different wild type strains of *Y. pestis* was differently. Additionally, the medium influenced the growth rate of the mutant strains (J Geng *et al.*, 2009; Bai *et al.*, 2010; Rempe *et al.*, 2012). A Δ*hfq* mutant in the *Y. pseudotuberculosis* IP32953 background did not show a growth defect (Schiano *et al.*, 2010) but preliminary data indicated, that deletion of *hfq* in the YPIII background influences growth (Heroven, unpublished).The growth of this Δ*hfq* mutant in the *Y. pseudotuberculosis* YPIII and IP32953 background was detected in BHI, LB, and DMEM medium. In BHI and LB medium the growth of both mutant strains was slightly impaired. This is consistent with the data published previously (J Geng *et al.*, 2009; Schiano *et al.*, 2010).

In minimal medium the growth of the Δ*hfq* mutant strains was reduced compared to the wild type, which stands in contrast to previously obtained data. It was reported, that the growth of a Δ*hfq* mutant in the IP32953 strain as well as in a *E. coli* Δ*hfq* mutant was not altered in minimal medium (Tsui *et al.*, 1994; Schiano *et al.*, 2010). It might be possible that suppressor mutants were built in minimal medium and therefore these strains did not show a significant growth defect. In *Y. pestis* a Δ*hfq* mutant shows a frequency of suppressor mutation between 10^{-3} to 10^{-6} (Bai *et al.*, 2010). This argument is supported by experiments performed during the work reported here, where the growth of both wild type and mutant strains was monitored in *Yersinia*-specific minimal medium containing glucose as only carbon source (M. Sest; data not shown). The Δ*hfq* mutant was either not able to grow in this medium or showed no significant growth defect compared to the wild type.

Further, the impact of Hfq on the physiology *of Y. pseudotuberculosis* YPIII was examined. To identify the role of *hfq* under different stress conditions, growth under osmotic, oxidative, and pH stress was monitored. Additionally, the influence of oxygen availability was determined. Alkaline and acidic pH did not influence the growth of a Δ*hfq* mutant strain. The exposure to osmotic stress and oxygen limitation did not influence the growth of the Δ*hfq* mutant, which was also shown in *Y. pestis*, *Salmonella* and *E. coli* (Tsui *et al.*, 1994; Sittka *et al.*, 2007; J Geng *et al.*, 2009).

When oxidative stress was introduced by the addition of H_2O_2 or paraquat, both wild type and the Δ*hfq* mutant showed a significant decrease in growth. Previous studies have shown that only 30-40 % of the bacteria survived treatment with 100 mM H_2O_2 after 30 min (Schiano *et al.*, 2010), indicating that most bacteria died during the growth experiments. Therefore, lower H_2O_2 and paraquat concentrations should be used in following experiments. Oxidative stress induced by diamide resulted in a strong growth defect of the Δ*hfq* mutant strain and lower Hfq protein levels in the stationary growth phase. This indicates that 1. Hfq is involved in the oxidative stress response and 2. *hfq* expression is controlled by oxidative stress.

Previously, it was reported that the Δ*hfq* mutant in the *Y. pseudotuberculosis* clinical isolate IP32953 shows a reduced intracellular survival in macrophages due to reduced survival after H_2O_2 stress (Schiano *et al.*, 2010). Together with the strong growth defect this indicates a need of Hfq for the survival under oxidative stress conditions. However, in contrast to the expectation Hfq protein levels were strongly reduced under diamide stress. One could

speculate, that the reduction of Hfq protein levels favors the interaction with sRNAs that have a very strong binding affinity. An sRNA regulating the response to oxidative stress would then preferentially bind to Hfq. Therefore, the wild type would be able to adapt under this stress condition but not an *hfq* mutant.

5 Outlook

In this study the identification of novel sRNAs in the human pathogen *Y. pseudotuberculosis* YPIII was reported using both 454 pyrosequencing and Illumina sequencing. In total, 169 sRNAs were identified by 454 sequencing classifying as *trans*-encoded sRNAs, *cis*-encoded antisense sRNAs, and mRNA leader structures, while an Illumina sequencing approach identified 83 *trans*-encoded and 80 *cis*-encoded antisense sRNAs. Additionally, Illumina sequencing was carried out for the global regulator mutant Δ*crp.* Only a subset of the sRNAs was expressed in the used environmental conditions. This became evident since nine sRNAs were only detectable in the Δ*crp* mutant. Identification of sRNAs under various other virulence-related conditions, e.g. host cell contact, or during an infection would broaden the spectrum of sRNAs and especially help to identify virulence-associated sRNAs. Sequencing of other global regulator mutants affecting the expression of virulence genes such as RpoS or GlnR would also help to identify the global set of sRNAs present in *Y. pseudotuberculosis*.

Further, the characterization of the role and function of selected candidates should be carried out. Therefore, mutant and overexpression strains need to be constructed. Subsequently, their molecular function and target identification could be examined. Additionally, the impact of some candidates on *Yersinia* virulence could be analyzed using the mouse model.

This study identified many Crp-dependent sRNAs. It would be interesting to further characterize the role of Crp on their expression. Band shift assays would unravel if direct or indirect regulation by Crp takes place. Additionally, it would be interesting to answer the question if Crp controls the expression of one or more maybe unknown factors, which are required for sRNAs expression and/or stability.

In *Y. pseudotuberculosis* the expression of *hfq* is not dependent on Crp and CsrA. To identify the regulatory cascade controlling *hfq* expression, a genebank screen could be performed. Additionally, Hfq was shown to be important for oxidative stress resistance. It would be interesting to identify how *hfq* expression is controlled by this stress and how Hfq regulates the oxidative stress response.

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7 Appendix

Table S 1: *trans*-encoded sRNAs detected by 454 sequencing. sRNAs with a seed region coverage above 10 reads are indicated in green. Chromosomally encoded sRNAs are indicated by a name YpseCxxxx, plasmid encoded sRNAs are indicated by YpsePxxxx.

Ypse	strand	start	stop	YPIII 25°C stat	YPIII 37°C exp	YP80 25°C stat	gene up-stream	gene down-stream	Sequence homologies	Rfam homo-logies	Identifica-tion by Woo *et al.*2011, Beauregard *et al.* 2012	Identification by Illumina sequencing
C0009	-	145659	145713	++	+		YPK_0120	YPK_0121	*Y. pseudotuberculosis*	no		
C0010	+	145981	146049	+			YPK_0120	YPK_0121	conserved in *Y. pestis*, *Y. pseudotuberculosis*	no		
C0028	+	358126	358256	+	+	+	YPK_0336	YPK_0337	γ-proteobacteria	no		
C0030	-	374173	374289	++++	+++	+++	YPK_0347	YPK_0348	γ-proteobacteria	TPP	Ysr52	YPK_transRNA_5
C0037	-	485421	485535	++	++++	++	YPK_0444	YPK_0445	γ-proteobacteria	no		
C0045	-	587218	587281	++++ ++	+		YPK_0532	YPK_0534	conserved in *Y. pestis*, *Y. pseudotuberculosis*	SraH		YPK_transRNA_8
C0050	-	611979	612060	+	+	+	YPK_0558	YPK_0560	conserved in *Y. pestis*, *Y. pseudotuberculosis*	no		
C0059	+	724935	725042	+		+	YPK_0662	YPK_0663	conserved in *Y. pestis*, *Y. pseudotuberculosis*	no		
C0060	-	819477	819603		+		YPK_0744	YPK_0745	γ-proteobacteria	no		
C0062	+	927416	927466		+	+	YPK_0811	YPK_0812	conserved in *Y. pestis*, *Y. pseudotuberculosis*	no		
C0065	-	984498	984693	++++ ++++	+++++	+++++ ++	YPK_0860	YPK_0861	γ-proteobacteria	6s	Ysr182	YPK_transRNA_15
C0066	+	1063996	1064047	+	+	+	YPK_0945	YPK_0946	conserved in *Y. pestis*, *Y. pseudotuberculosis*	no		
C0067	+	1154479	1154574	+	+		YPK_1026	YPK_1027	conserved in *Yersinia*	SraE, OmrA/B,	Ysr148	YPK_transRNA_16
C0068	-	1189054	1189263	++++ +	+++++	+++++ ++	YPK_1051	YPK_1052	γ-proteobacteria	GcvB	Ysr45	YPK_transRNA_18
C0069	+	1196497	1196800	++	+	++	YPK_1058	YPK_1059	γ-proteobacteria	CsrB	Ysr179	YPK_transRNA_19
C0073	+	1208942	1208997	++	++	++	YPK_1070	YPK_1071	conserved in *Y. pestis*, *Y. pseudotuberculosis*	no		
C0075	+	1236002	1236056	+	+++	+	YPK_1097	YPK_R0085	conserved in *Y. pestis*, *Y. pseudotuberculosis*	no		
C0076	+	1263048	1263157	+	+	+	YPK_1123	YPK_1124	conserved in *Yersinia*	no		
C0077	-	1279354	1279446	++	+	+	YPK_1140	YPK_1141	conserved in *Y. pestis*, *Y. pseudotuberculosis*	no		
C0078	+	1300427	1300518	+		+	YPK_1159	YPK_1160	conserved in *Y. pestis*, *Y. pseudotuberculosis*	no		
C0083	+	1346533	1346613	+++	+++++	+++	YPK_1215	YPK_1216	only YPIII	no		
C0085	+	1384235	1384557	++++ ++	++++	++++	YPK_1255	YPK_1256	γ-proteobacteria	GlmY	Ysr147	YPK_transRNA_22
C0090	+	1450270	1450326	+	+	+	YPK_1319	YPK_1320	conserved in *Y. pestis*, *Y. pseudotuberculosis*	no		
C0091	-	1454604	1454710	++++ +++	++	++	YPK_1324	YPK_1325	conserved in *Y. pestis*, *Y. pseudotuberculosis*	CyaR, RyeE	Ysr159	YPK_transRNA_25
C0093	-	1578446	1578529	+	+	+	YPK_1428	YPK_1429	conserved in *Y. pestis*, *Y. pseudotuberculosis*	no		
C0098	+	1683385	1683438	+		+	YPK_1520	YPK_1521	conserved in *Y. pestis*, *Y. pseudotuberculosis*	no		
C0099	+	1700376	1700505	+		+	YPK_1537	YPK_1538	conserved in *Y. pestis*, *Y. pseudotuberculosis*	no		
C0104	-	1754266	1754352	(+)		+	YPK_1585	YPK_1586	conserved in *Y. pestis*, *Y. pseudotuberculosis*	no		
C0106	+	1785904	1785970	(+)	(+)	+	YPK_1614	YPK_1615	*Y. pseudotuberculosis*	no		
C0108	+	1819568	1819626	++	+++	++	YPK_1640	YPK_1641	conserved in *Y. pestis*, *Y. pseudotuberculosis*	no	Ysr20	
C0109	-	1837359	1837464	++	(+)	+	YPK_1654	YPK_1655	conserved in *Y. pestis*, *Y. pseudotuberculosis*	no	Ysr164	YPK_transRNA_27
C0118	-	1919698	1919776	+	++		YPK_1730	YPK_1731	conserved in *Y. pestis*, *Y. pseudotuberculosis*	no		

Ypse	strand	start	stop	YPIII 25°C stat	YPIII 37°C exp	YP80 25°C stat	gene up-stream	gene down-stream	Sequence homologies	Rfam homo-logies	Identifica-tion by Woo *et al.*2011, Beauregard *et al.* 2012	Identification by Illumina sequencing
C0120	+	1936536	1936588	+	+	+	YPK_1744	YPK_1745	conserved in *Y. pestis*, *Y. pseudotuberculosis*	no		
C0124	+	2009366	2009418	+	+		YPK_1808	YPK_1809	conserved in *Y. pestis*, *Y. pseudotuberculosis*	no		
C0125	-	2017411	2017501	++++ ++++	+++++ +	+++++	YPK_1818	YPK_1819	conserved in *Y. pestis*, *Y. pseudotuberculosis*	no		YPK_transRNA_30
C0126	+	2018521	2018573	+	(+)	+	YPK_1819	YPK_1820	conserved in *Y. pestis*, *Y. pseudotuberculosis*	no		
C0136	+	2100452	2100565	++++ +	++	++++	YPK_1892	YPK_1893	γ-proteobacteria	RyhB	Ysr146	YPK_transRNA_34
C0137	+	2114912	2115036	+++	++	++	YPK_1907	YPK_1908	γ-proteobacteria	no	Ysr11	
C0139	+	2161355	2161497	+	(+)	+	YPK_1946	YPK_1947	conserved in *Y. pestis*, *Y. pseudotuberculosis*	no		YPK_transRNA_35
C0140	-	2167036	2167143	+		+	YPK_1950	YPK_1951	conserved in *Y. pestis*, *Y. pseudotuberculosis*	no		YPK_transRNA_36
C0155	-	2376073	2376124		+	+	YPK_2144	YPK_2145	conserved in *Y. pestis*, *Y. pseudotuberculosis*	no		
C0167	-	2668685	2668802	++++ +++	+	++	YPK_2434	YPK_2435	γ-proteobacteria	RyeB	+	YPK_transRNA_44
C0168	-	2670797	2670878		(+)	+	YPK_2437	YPK_2438	conserved in *Y. pestis*, *Y. pseudotuberculosis*	no		
C0169	+	2683152	2683216	+	+	(+)	YPK_2450	YPK_2451	conserved in *Y. pestis*, *Y. pseudotuberculosis*	no		
C0170	+	2701574	2701686	++	++++	+	YPK_2467	YPK_2468	γ-proteobacteria	no		
C0172	+	2735922	2735986	+		+	YPK_2501	YPK_2502	conserved in *Y. pestis*, *Y. pseudotuberculosis*	no		
C0174	-	2818717	2818797	+	+	+	YPK_2566	YPK_2567	conserved in *Y. pestis*, *Y. pseudotuberculosis*	no		
C0177	-	2892613	2892902	++++		++++	YPK_2635	YPK_2637	γ-proteobacteria	no		YPK_transRNA_50
C0179	-	2928791	2928902	++	+	++	YPK_2662	YPK_2663	conserved in *Y. pestis*, *Y. pseudotuberculosis*	no		
C0182	-	2966577	2966663	+		++	YPK_2687	YPK_2688	conserved in *Y. pestis*, *Y. pseudotuberculosis*	no	Ysr114	
C0184	+	2975339	2975453	+		+	YPK_2693	YPK_2695	conserved in *Y. pestis*, *Y. pseudotuberculosis*	no		
C0185	+	3015959	3016048	++++ ++	++++	++++	YPK_2734	YPK_2735	γ-proteobacteria	RybB		YPK_transRNA_53
C0186	+	3072179	3072300	+	+		YPK_2783	YPK_2784	conserved in *Y. pestis*, *Y. pseudotuberculosis*	no		
C0189	+	3119618	3119714	+	+	+	YPK_2834	YPK_2836	conserved in *Y. pestis*, *Y. pseudotuberculosis*	no	Ysr62	YPK_transRNA_54
C0193	+	3152490	3152546	+	(+)		YPK_2857	YPK_2858	conserved in *Y. pestis*, *Y. pseudotuberculosis*	no		
C0195	-	3192526	3192593	+	+	+	YPK_2898	YPK_2899	conserved in *Y. pestis*, *Y. pseudotuberculosis*	no		
C0199	+	3279863	3280243	++++ ++	+++	+++++ +	YPK_2980	YPK_2981	γ-proteobacteria	tmRNA	+	YPK_transRNA_57
C0201	+	3293752	3293872	++	+++	+	YPK_2995	YPK_2996	γ-proteobacteria	STnc490k		
C0203	-	3303801	3303882	+	+	+	YPK_R0033	YPK_3004	conserved in *Y. pestis*, *Y. pseudotuberculosis*	no		
C0205	-	3326406	3326484	+	+		YPK_3023	YPK_3024	conserved in *Y. pestis*, *Y. pseudotuberculosis*	no		
C0209	+	3407406	3407474	++	(+)		YPK_3109	YPK_3110	only YPIII	no		YPK_transRNA_59
C0210	-	3443683	3443743	++	++	++	YPK_3148	YPK_3149	only YPIII	no		
C0211	+	3448464	3448515	+	+		YPK_3152	YPK_3153	conserved in *Y. pestis*, *Y. pseudotuberculosis*	no		
C0212	-	3463919	3464025	++++ +++	+++++ +	++++	YPK_3165	YPK_3167	conserved in *Y. pestis*, *Y. pseudotuberculosis*	MicM	Ysr145	YPK_transRNA_60
C0214	-	3515595	3515739	++++	++++	+++	YPK_3214	YPK_3215	γ-proteobacteria	SRP bact	+	YPK_transRNA_61
C0216	-	3533160	3533235	+	+	(+)	YPK_3230	YPK_3231	conserved in *Y. pestis*, *Y. pseudotuberculosis*	no		
C0226	-	3619350	3619456	+	+	+	YPK_3305	YPK_3306	conserved in *Y. pestis*, *Y. pseudotuberculosis*	no		
C0228	-	3673752	3673929		++		YPK_R0091	YPK_3349	conserved in *Yersinia*	no		YPK_transRNA_63
C0233	+	3694599	3694670	++	+	+	YPK_3368	YPK_3370	γ-proteobacteria	MicA	Ysr7	YPK_transRNA_65

Ypse	strand	start	stop	YPIII 25°C stat	YPIII 37°C exp	YP80 25°C stat	gene up-stream	gene down-stream	Sequence homologies	Rfam homo-logies	Identifica-tion by Woo *et al.*2011, Beauregard *et al.* 2012	Identification by Illumina sequencing
C0243	-	3789292	3789380	(+)	+	+	YPK_3451	YPK_3452	conserved in *Y. pestis, Y. pseudotuberculosis*	no		
C0248	-	3853065	3853158	+	+	+	YPK_3508	YPK_3509	conserved in *Yersinia*	no		YPK_transRNA_69
C0250	-	3892233	3892285	+			YPK_3539	YPK_3540	conserved in *Y. pestis, Y. pseudotuberculosis*	no	Ysr150	
C0261	-	4009176	4009238	+			YPK_3631	YPK_3633	conserved in *Y. pestis, Y. pseudotuberculosis*	no		
C0262	-	4023679	4023831	++		+	YPK_3644	YPK_3645	conserved in *Y. pestis, Y. pseudotuberculosis*	no		YPK_transRNA_72
C0273	+	4210860	4210998	++	(+)	(+)	YPK_3821	YPK_3822	γ-proteobacteria	no		
C0274	-	4210860	4211028	+	+	+	YPK_3821	YPK_3822	γ-proteobacteria	no		
C0278	+	4240106	4240156	+	+		YPK_3850	YPK_3852	conserved in *Y. pestis, Y. pseudotuberculosis*	no		
C0279	-	4249415	4249582	++	+	++	YPK_3856	YPK_3857	conserved in *Y. pestis, Y. pseudotuberculosis*	no	Ysr100	YPK_transRNA_74
C0281	-	4320477	4320530		+		YPK_3920	YPK_3921	conserved in *Y. pestis, Y. pseudotuberculosis*	no		
C0283	-	4432511	4432736	++++ ++	+++	++	YPK_4019	YPK_R0045	conserved in *Yersinia*	GlmZ	Ysr148	YPK_transRNA_75
C0284	-	4451476	4451545	+	+	+	YPK_4034	YPK_4035	conserved in *Yersinia*	no		
C0285	-	4510606	4510660		+		YPK_4084	YPK_4085	conserved in *Y. pestis, Y. pseudotuberculosis*	no		
C0294	-	4629444	4629551	++	++++	+++	YPK_4194	YPK_4195	γ-proteobacteria	Spot42	Ysr185	YPK_transRNA_81
C0296	-	4643352	4643432	+	(+)	(+)	YPK_R0088	YPK_4206	γ-proteobacteria	no		
C0298	+	4665974	4666049	+	+	+	YPK_4227	YPK_4228	conserved in *Y. pestis, Y. pseudotuberculosis*	no		
C0300	-	4688906	4688989	(+)	+		YPK_4249	YPK_4250	conserved in *Y. pestis, Y. pseudotuberculosis*	no		
P0003	-	17236	17335	+	+++	+	pYV0020	pYV0021	conserved in *Yersinia*	no		
P0016	+	4240	4314		(+)		pYV0004	pYV0005	conserved in *Yersinia*	no		
P0017	+	29371	29409	+	+++	+	pYV0040	pYV0041	conserved in *Yersinia*	no		

Table S 2: *cis*-encoded antisense sRNAs detected by 454 sequencing. sRNAs with a seed region coverage above 10 reads are indicated in green. Chromosomally encoded sRNAs are indicated by a name YpseCxxxx, plasmid encoded sRNAs are indicated by YpsePxxxx.

Ypse	strand	start	stop	YPIII 25°C stat	YPIII 37°C exp	YP80 25°C stat	gene cis	Sequence homologies	Rfam homo-logies	Identification by Woo *et al.*2011, Beauregard *et al.* 2012	Identification by Illumina sequencing
C0013	+	206360	206417		+		YPK_0160	conserved in *Y. pestis, Y. pseudotuberculosis*	no		
C0015	+	252844	253016	+++	+	+++	YPK_0215	only YPIII	no		YPK_asRNA_2
C0032	+	408707	408766		+		YPK_0374	conserved in *Y. pestis, Y. pseudotuberculosis*	no		
C0035	-	418299	418381	+		+	YPK_0383	conserved in *Y. pestis, Y. pseudotuberculosis*	no		YPK_asRNA_4
C0036	-	481502	481567	++	+	+	YPK_0438	conserved in *Y. pestis, Y. pseudotuberculosis*	no		
C0046	-	593452	593510		+	+	YPK_0540	conserved in *Yersinia*	no		
C0054	-	679976	680026	++	+	++	YPK_0618	only YPIII	no		
C0055	-	680705	680777	+	++	+	YPK_0619	only YPIII	no		
C0058	+	709558	709723	+	++	+	YPK_0648	γ-proteobacteria	FMN		
C0063	+	934693	934764	(+)	+		YPK_0817	conserved in *Y. pestis, Y. pseudotuberculosis*	no		
C0081	+	1333751	1333812	+++		+	YPK_1198	only YPIII	no		YPK_asRNA_9
C0100	+	1714561	1714631	+	+	+	YPK_1551	γ-proteobacteria	no		
C0123	+	2008218	2008318	+			YPK_1807	conserved in *Y. pestis, Y. pseudotuberculosis*	no		
C0135	+	2094312	2094455	+			YPK_1887	conserved in *Y. pestis, Y. pseudotuberculosis*	no		
C0146	-	2234841	2234920	+	+	+	YPK_2007	conserved in *Y. pestis, Y. pseudotuberculosis*	no		YPK_asRNA_20
C0147	+	2237806	2237867	+	+	+	YPK_2009	conserved in *Y. pestis, Y. pseudotuberculosis*	no		
C0153	+	2372009	2372058	+			YPK_2140	conserved in *Yersinia*	no		
C0154	+	2372267	2372340	(+)	+	(+)	YPK_2140	conserved in *Yersinia*	no		
C0161	-	2478893	2479082	++	++++	+	YPK_2234	γ-proteobacteria	STnc490k		
C0162	+	2492353	2492428		+++	+	YPK_2245	conserved in *Y. pestis, Y. pseudotuberculosis*	no		
C0175	+	2870864	2870936	+	+	++	YPK_2615	conserved in *Y. pestis, Y. pseudotuberculosis*	no		
C0176	-	2886823	2887006	++	++++	+	YPK_2631	γ-proteobacteria	Stnc490k		

Ypse	strand	start	stop	YPIII 25°C stat	YPIII 37°C exp	YP80 25°C stat	gene cis	Sequence homologies	Rfam homo-logies	Identification by Woo *et al.*2011, Beauregard *et al.* 2012	Identification by Illumina sequencing
C0180	+	2964693	2964767		+	+	YPK_2686	conserved in *Y. pestis, Y. pseudotuberculosis*	no		
C0190	+	3126116	3126204	++	++++		YPK_2840	conserved in *Y. pestis, Y. pseudotuberculosis*	no		
C0191	-	3138126	3138204			+	YPK_2847	conserved in *Y. pestis, Y. pseudotuberculosis*	no		
C0208	-	3356423	3356473		+	(+)	YPK_3053	conserved in *Y. pestis, Y. pseudotuberculosis*	no		
C0222	+	3593022	3593117	(+)	+	+	YPK_3282	conserved in *Y. pestis, Y. pseudotuberculosis*	no		YPK_asRNA_40
C0225	-	3603949	3604026	++	+	+	YPK_3293	conserved in *Y. pestis, Y. pseudotuberculosis*	no		YPK_asRNA_41
C0230	+	3678439	3678524		++		YPK_3352	γ-proteobacteria	no		
C0231	-	3679100	3679167	+	+	+	YPK_3352	γ-proteobacteria	no		YPK_asRNA_43
C0246	-	3825281	3825355		+	+	YPK_3482	conserved in *Y. pestis, Y. pseudotuberculosis*	no		
C0247	-	3849561	3849631	(+)	+	(+)	YPK_3501	conserved in *Yersinia*	no		
C0251	+	3922218	3922290	+	(+)		YPK_3560	conserved in *Y. pestis, Y. pseudotuberculosis*	no		
C0259	-	3980285	3980375	+		++	YPK_3609	conserved in *Y. pestis, Y. pseudotuberculosis*	no		
C0286	+	4510609	4510694	(+)	++		YPK_4085	conserved in *Y. pestis, Y. pseudotuberculosis*	no		
C0293	-	4597204	4597278	+++++ +	++++	++	YPK_4167	conserved in *Y. pestis, Y. pseudotuberculosis*	no		
P0001	+	1770	1850	++	+	+	pYV0001	conserved in *Yersinia*	no		YPKp_asRNA_3
P0004	+	19070	19139	+++	+	++	pYV0022	γ-proteobacteria	no		YPKp_asRNA_5
P0011	-	55960	56042	++	+++	++	pYV0079	conserved in *Yersinia*	no		YPKp_asRNA_11
P0015	+	66817	66932	++++	++++	++++		γ-proteobacteria	no		
P0018	+	39192	39286	+	+		pYV0057	conserved in *Yersinia*	no		
P0019	+	43865	44003		+		pYV0063	conserved in *Yersinia*	no		
P0020	+	44987	45229		+		pYV0065	conserved in *Yersinia*	no		

Table S 3: Results of the 454 sequencing for *cis*-encoded sense sRNAs. Bioinformatic parameters: size 50-500 nts, permanent coverage 5 reads. Chromosomally encoded sRNAs are indicated by a name YpseCxxxx, plasmid encoded sRNAs are indicated by YpsePxxxx. These sRNAs were only detected after bioinformatic analysis with low stringent criteria.

Ypse	strand	start	stop	YPIII 25°C stat	YPIII 37°C exp	YP80 25°C stat	gene cis	Sequence homologies	Rfam homo-logies	Identifica-tion by Woo *et al.*2011, Beaure-gard *et al.* 2012	Identifica-tion by Illumina sequencing
C0001	+	1877	1994			+	YPK_0002	γ-proteobacteria	no		
C0002	-	38044	38162	++	+	+	YPK_0035	conserved in *Y. pestis, Y. pseudotuberculosis*	no		
C0004	+	43375	43466	++	+	+	YPK_0039	γ-proteobacteria	no		
C0006	-	145003	145063	++	+	++	YPK_0120	conserved in *Y. pestis, Y. pseudotuberculosis*	no		
C0007	-	145068	145120	++	+	++	YPK_0120	conserved in *Y. pestis, Y. pseudotuberculosis*	no		
C0008	-	145173	145230	++	+	++	YPK_0120	conserved in *Y. pestis, Y. pseudotuberculosis*	no		
C0011	-	146518	146631		+	++	YPK_0122	conserved in *Y. pestis, Y. pseudotuberculosis*	no		
C0012	-	204390	204480	++	+	++	YPK_0158	conserved in *Y. pestis, Y. pseudotuberculosis*	no		
C0016	+	312342	312397			+	YPK_0273	conserved in *Y. pestis, Y. pseudotuberculosis*	no		
C0019	+	317183	317360	++	+	++	YPK_0278	γ-proteobacteria	no		
C0020	+	324240	324360	+	++	+	YPK_0292	γ-proteobacteria	no		
C0024	+	328696	328755	+	++		YPK_0303	γ-proteobacteria	no		
C0029	+	359329	359432		+		YPK_0338	γ-proteobacteria	P26	Ysr51	
C0031	-	390059	390125	++			YPK_0362	conserved in *Y. pestis, Y. pseudotuberculosis*	no		
C0033	-	409277	409533	+++		+++	YPK_0376	γ-proteobacteria	no		
C0034	+	417663	417748	+			YPK_0382	conserved in *Y. pestis, Y. pseudotuberculosis*	no		
C0041	-	555444	555521		+		YPK_0503	conserved in *Y. pestis, Y. pseudotuberculosis*	no		
C0042	-	556977	557050	+	(+)	+	YPK_0505	conserved in *Y. pestis, Y. pseudotuberculosis*	no		
C0047	+	593903	594285	+++++ +	+++++ +	++++++	RNaseP	γ-proteobacteria	RnaseP	Ysr151	YPK_transRNA_09
C0049	-	610506	610614	+	+	+	YPK_0558	conserved in *Y. pestis, Y. pseudotuberculosis*	no		
C0051	-	614267	614341	+	+		YPK_0561	conserved in *Y. pestis, Y. pseudotuberculosis*	no		
C0057	-	691366	691500	+	+	+	YPK_0634	γ-proteobacteria	no		
C0061	+	826676	826790	+	++	+	YPK_0749	conserved in *Y. pestis, Y. pseudotuberculosis*	no		
C0064	+	983535	983745	++	+	++	YPK_0859	conserved in *Yersinia*	no		
C0071	+	1205805	1205883		+		YPK_1067	γ-proteobacteria	no		

Ypse	strand	start	stop	YPIII 25°C stat	YPIII 37°C exp	YP80 25°C stat	gene cis	Sequence homologies	Rfam homo-logies	Identifica-tion by Woo *et al.*2011, Beaure-gard *et al*. 2012	Identifica-tion by Illumina sequencing
C0072	+	1208206	1208278	+	++	(+)	YPK_1070	conserved in *Y. pestis, Y. pseudotuberculosis*	no		
C0074	+	1215933	1216008	+	+	+	YPK_1076	conserved in *Y. pestis, Y. pseudotuberculosis*	no		
C0080	+	1319996	1320087	++	+	+	YPK_1184	conserved in *Y. pestis, Y. pseudotuberculosis*	no		
C0082	+	1345744	1345810	+	+	+	YPK_1214	only YPIII	no		
C0084	-	1346703	1346781		+		YPK_1216	only YPIII	no		
C0086	+	1385864	1385947		++		YPK_1257	conserved in *Y. pestis, Y. pseudotuberculosis*	no		
C0088	+	1396156	1396441	+	+++	+	YPK_1268	conserved in *Y. pestis, Y. pseudotuberculosis*	no		
C0089	+	1420978	1421084	+	+	+	YPK_1291	conserved in *Y. pestis, Y. pseudotuberculosis*	no		
C0092	-	1510416	1510471	+	(+)		YPK_1371	conserved in *Y. pestis, Y. pseudotuberculosis*	no		
C0094	-	1579882	1580003	+			YPK_1430	conserved in *Y. pestis, Y. pseudotuberculosis*	no		
C0102	+	1723686	1723893	+++	+	+++	YPK_1559	conserved in *Yersinia*	no		
C0105	+	1776292	1776373	+	+	(+)	YPK_1606	conserved in *Y. pestis, Y. pseudotuberculosis*	no		
C0107	+	1805398	1805450	+	+	+	YPK_1626	only YPIII	no		
C0113	+	1868601	1868769	+	++		YPK_1681	conserved in *Yersinia*	no		
C0115	+	1872558	1872714	++	+	+	YPK_1686	γ-proteobacteria	no		
C0122	-	1973551	1973625	+	++	++	YPK_1779	conserved in *Y. pestis, Y. pseudotuberculosis*	no		
C0127	+	2020438	2020599	++	++	+	YPK_1820	conserved in *Yersinia*	no		
C0129	+	2021697	2021894	+	++	+	YPK_1823	γ-proteobacteria	no		
C0132	-	2063844	2063900	(+)	+		YPK_1856	conserved in Y. *pestis, Y. pseudotuberculosis*	no		
C0133	+	2087626	2087705	+++	++	++	YPK_1881	conserved in *Y. pestis, Y. pseudotuberculosis*	no		
C0138	-	2124961	2125022	++		+++	YPK_1917	conserved in *Y. pestis, Y. pseudotuberculosis*	no		
C0143	+	2194759	2194810	+			YPK_1975	only *Y. pseudotuberculosis*	no		
C0144	+	2204516	2204592	+	+	+	YPK_1983	conserved in *Y. pestis, Y. pseudotuberculosis*	no		
C0145	+	2234835	2234923	+	+	+	YPK_2007	conserved in *Y. pestis, Y. pseudotuberculosis*	no		
C0149	-	2328128	2328196	(+)	+		YPK_2098	conserved in *Y. pestis, Y. pseudotuberculosis*	no		
C0150	-	2355578	2355709	+	+	+	YPK_2125	γ-proteobacteria	no		
C0151	-	2371353	2371424	+	++	+	YPK_2139	conserved in *Yersinia*	no		
C0152	-	2371687	2371830	+++	++	+++	YPK_2140	conserved in *Y. pestis, Y. pseudotuberculosis*	no		
C0158	+	2438276	2438446	(+)		+	YPK_2200	conserved in *Y. pestis, Y. pseudotuberculosis*	no		
C0159	-	2465875	2465960			++	YPK_2224	conserved *in Y. pestis, Y. pseudotuberculosis*	no		
C0163	+	2579696	2579753		+		YPK_2346	only YPIII	no		
C0164	-	2588563	2588661	+		(+)	YPK_2355	conserved in *Y. pestis, Y. pseudotuberculosis*	no		
C0178	+	2912156	2912226	+		+	YPK_2649	conserved in *Y. pestis, Y. pseudotuberculosis*	no		
C0192	+	3140969	3141072	+	+	+	YPK_2848	conserved in *Y. pestis, Y. pseudotuberculosis*	no		
C0194	+	3166542	3166666		+	(+)	YPK_2868	conserved in *Y. pestis, Y. pseudotuberculosis*	no		
C0197	-	3253693	3253772		+	(+)	YPK_2954	γ-proteobacteria	no		
C0202	+	3297199	3297373		+		YPK_2998	conserved in *Y. pestis, Y. pseudotuberculosis*	no		
C0204	+	3312893	3312992	++	(+)	+	YPK_3010	conserved in *Y. pestis, Y. pseudotuberculosis*	no		
C0206	-	3332269	3332584	+++++ ++	++	++++++	YPK_3031	γ-proteobacteria	no		
C0213	-	3497537	3497640		+	(+)	YPK_3198	conserved in *Y. pestis, Y. pseudotuberculosis*	no		
C0218	+	3541718	3541773	+			YPK_3238	conserved in *Y. pestis, Y. pseudotuberculosis*	no		
C0219	+	3549453	3549519	+	+	+	YPK_3245	conserved in *Y. pestis, Y. pseudotuberculosis*	no		
C0220	-	3567955	3568037		+		YPK_3263	γ-proteobacteria	no		
C0235	+	3747950	3748002	+		(+)	YPK_3416	conserved in *Y. pestis, Y. pseudotuberculosis*	no		
C0236	-	3759259	3759308			+	YPK_3425	γ-proteobacteria	no		
C0237	-	3760653	3760780	+++	++	++	YPK_3426	conserved in *Yersinia*	no		
C0239	-	3779796	3779889	(+)	(+)	+	YPK_3446	γ-proteobacteria	no		
C0241	-	3781088	3781252	++	(+)	(+)	YPK_3447	γ-proteobacteria	no		
C0242	-	3781268	3781357			+	YPK_3447	conserved in *Y. pestis, Y. pseudotuberculosis*	no		
C0244	-	3806181	3806322	+	+	+	YPK_3464	conserved in *Y. pestis, Y. pseudotuberculosis*	no		
C0252	-	3925579	3925695			+	YPK_3563	conserved in *Y. pestis, Y. pseudotuberculosis*	no		
C0253	+	3929681	3929796			+	YPK_3567	conserved in *Y. pestis, Y. pseudotuberculosis*	no		
C0254	+	3938657	3938736	++	+	+	YPK_3573	γ-proteobacteria	no		

Ypse	strand	start	stop	YPIII 25°C stat	YPIII 37°C exp	YP80 25°C stat	gene cis	Sequence homologies	Rfam homo-logies	Identifica-tion by Woo *et al.*2011, Beaure-gard *et al*. 2012	Identifica-tion by Illumina sequencing
C0255	-	3944744	3944810	+	++	+	YPK_3582	conserved in *Y. pestis, Y. pseudotuberculosis*	no		
C0263	+	4068890	4068939	+			YPK_3681	conserved in *Y. pestis, Y. pseudotuberculosis*	no		
C0265	-	4102257	4102334	+	+	+	YPK_3714	conserved in *Y. pestis, Y. pseudotuberculosis*	no		
C0266	-	4118590	4118703	+++	+++	++	YPK_3727	conserved in *Yersinia*	no		
C0271	-	4186254	4186362		+	(+)	YPK_3798	γ-proteobacteria	no		
C0275	-	4211250	4211338		+		YPK_3822	conserved in *Y. pestis, Y. pseudotuberculosis*	no		
C0277	+	4216021	4216105		+	+	YPK_3825	conserved in *Y. pestis, Y. pseudotuberculosis*	no		
C0280	+	4260400	4260494	+			YPK_3865	conserved in *Y. pestis, Y. pseudotuberculosis*	no		
C0282	-	4336223	4336298	+	(+)		YPK_3931	conserved in *Y. pestis, Y. pseudotuberculosis*	no		
C0287	-	4515176	4515243	+	(+)	+	YPK_4087	conserved in *Y. pestis, Y. pseudotuberculosis*	no		
C0289	+	4537170	4537242	++	++	++		conserved in *Y. pestis, Y. pseudotuberculosis*	no		
C0292	-	4586495	4586649	+	+	+	YPK_4155	γ-proteobacteria	no		
P0006	+	21056	21122		+		pYV0025	conserved in *Yersinia*	no		
P0007	+	21154	21229		+		pYV0025	conserved in *Yersinia*	no		
P0009	-	21775	21842	+	+	++	pYV0027	conserved in *Yersinia*	no		
P0012	+	55991	56043		+		pYV0079	conserved in *Yersinia*	no		
P0013	+	59059	59130		+		pYV0084	conserved in *Yersinia*	no		
P0014	-	64921	64971	+	+	+	pYV0094	conserved in *Yersinia*	no		

Table S 4: mRNA leader structures identified by 454 sequencing. All mRNA leader structures were identified with both thresholds. Chromosomally encoded sRNAs are indicated by a name YpseCxxxx, plasmid encoded sRNAs are indicated by YpsePxxxx.

Ypse	strand	start	stop	YPIII 25°C stat	YPIII 37°C exp	YP80 25°C stat	gene cis	Sequence homologies	Rfam homo-logies
C0003	-	40031	40081		++		-	conserved in *Yersinia*	no
C0005	+	55481	55597			++	YPK_0051	conserved in *Y. pestis, Y. pseudotuberculosis*	no
C0014	-	227322	227396	+		++	YPK_0174	conserved in *Y. pestis, Y. pseudotuberculosis*	no
C0017	+	312758	312964	+	+++	+	YPK_0275	γ-proteobacteria	no
C0018	+	315975	316106	+	++		YPK_0277	γ-proteobacteria	no
C0021	+	324410	324599	+	++		YPK_0293	γ-proteobacteria	no
C0022	+	324746	324809	+	++		YPK_0293	γ-proteobacteria	no
C0023	+	325634	325696	+	++		YPK_0295	γ-proteobacteria	no
C0025	+	330074	330144		+		YPK_0305	γ-proteobacteria	Alpha RBS
C0026	+	340233	340345	+++	+++	+++	YPK_0317	γ-proteobacteria	no
C0027	+	357236	357347	+			YPK_0335	γ-proteobacteria	no
C0038	-	486362	486457	+	+	+	YPK_0445	conserved in *Y. pestis, Y. pseudotuberculosis*	no
C0039	-	501184	501302		+		YPK_0460	conserved in *Yersinia*	no
C0040	-	551494	551606	+		++	YPK_0497	conserved in *Y. pestis, Y. pseudotuberculosis*	no
C0043	+	573205	573364	+	++	+	YPK_0524	γ-proteobacteria	no
C0044	+	573690	573762		+		YPK_0525	γ-proteobacteria	no
C0048	-	599208	599259	+	(+)		YPK_0547	conserved in *Y. pestis, Y. pseudotuberculosis*	no
C0052	-	663704	663765	+			YPK_0598	only YPIII and IP31758	no
C0053	+	676595	676674	+	+	+	YPK_0614	only YPIII	no
C0056	+	689091	689181	+		+	YPK_0631	only YPIII	no
C0070	+	1203902	1204141		++		YPK_1066	conserved in *Yersinia*	t44
C0079	+	1318517	1318608	+	+	+	YPK_1182	conserved in *Yersinia*	no
C0087	+	1395762	1396089	+	+++	+	YPK_1268	conserved in Yersinia	no
C0095	+	1580707	1580890	+	(+)	(+)	YPK_1431	γ-proteobacteria	no
C0096	+	1597941	1598006	+	+	+	YPK_1446	γ-proteobacteria	no
C0097	-	1667968	1668060	+	++	++	YPK_1506	conserved in *Y. pestis, Y. pseudotuberculosis*	no
C0101	+	1722949	1723235	+++	++	++++++	YPK_1559	conserved in *Yersinia*	no
C0103	+	1724462	1724663	+	+	+	YPK_1560	γ-proteobacteria	no
C0110	-	1842869	1842973	+	(+)	+	YPK_1659	*Y. pseudotuberculosis*	no
C0111	-	1858774	1859025	+++	+	+	YPK_1673	conserved in *Yersinia*	no
C0112	+	1868497	1868564		++	(+)	YPK_1681	γ-proteobacteria	no
C0114	+	1869003	1869065	+	+	(+)	YPK_1681	γ-proteobacteria	no
C0116	+	1873143	1873198	+	+	+	YPK_1687	γ-proteobacteria	no
C0117	-	1905102	1905177	+	+	++	YPK_1715	conserved in *Y. pestis, Y. pseudotuberculosis*	no
C0119	+	1928117	1928355	+	+++++	+	YPK_1740	γ-proteobacteria	no
C0121	+	1955920	1956027	+		++	YPK_1761	conserved in *Y. pestis, Y. pseudotuberculosis*	no
C0128	+	2021174	2021223	(+)	+		YPK_1821	conserved in *Y. pestis, Y. pseudotuberculosis*	no
C0130	+	2025578	2025788	++	+	++	YPK_1826	γ-proteobacteria	no
C0131	-	2059684	2059944	++++	++	++	YPK_1854	γ-proteobacteria	no

Ypse	strand	start	stop	YPIII 25°C stat	YPIII 37°C exp	YP80 25°C stat	gene cis	Sequence homologies	Rfam homo-logies
C0134	-	2090666	2090779	+		+	YPK_1885	conserved in *Y. pestis, Y. pseudotuberculosis*	no
C0141	-	2173138	2173189		+	+	YPK_1954	conserved in *Y. pestis, Y. pseudotuberculosis*	no
C0142	-	2184837	2184890		+	(+)	YPK_1966	*Y. pseudotuberculosis*	no
C0148	+	2280261	2280424	+++	+	++	YPK_2048	conserved in *Y. pestis, Y. pseudotuberculosis*	no
C0156	+	2381803	2381938	+	(+)	(+)	YPK_2150	conserved in *Yersinia*	no
C0157	-	2385207	2385329	+	(+)	++	YPK_2153	conserved in *Y. pestis, Y. pseudotuberculosis*	no
C0160	-	2466021	2466186			++	YPK_2224	conserved in *Y. pestis, Y. pseudotuberculosis*	no
C0165	-	2615775	2615868	+		++	YPK_2381	conserved in *Y. pestis, Y. pseudotuberculosis*	no
C0166	-	2624408	2624474	+	+	+	YPK_2389	conserved in *Y. pestis, Y. pseudotuberculosis*	no
C0171	-	2710217	2710286		(+)	+	YPK_2474	γ-proteobacteria	no
C0173	-	2799717	2799769	+	+	+	YPK_2552	conserved in *Y. pestis, Y. pseudotuberculosis*	no
C0181	-	2964701	2964759	(+)	+	+	YPK_2686	conserved in *Y. pestis, Y. pseudotuberculosis*	no
C0183	+	2974959	2975138	++++++	+	++	YPK_2694	γ-proteobacteria	no
C0187	-	3081112	3081274	++++	(+)	+	YPK_2790	conserved in *Y. pestis, Y. pseudotuberculosis*	no
C0188	+	3086567	3086727	+	+++	+	YPK_2795	γ-proteobacteria	no
C0196	-	3236994	3237083	+	++	++	YPK_2938	conserved in *Y. pestis, Y. pseudotuberculosis*	no
C0198	-	3272442	3272596	++	++	++	YPK_2972	γ-proteobacteria	no
C0200	+	3285221	3285293	+	+	(+)	YPK_2991	conserved in *Y. pestis, Y. pseudotuberculosis*	no
C0207	-	3336046	3336152	+	(+)	+	YPK_3035	conserved in *Y. pestis, Y. pseudotuberculosis*	no
C0215	-	3516961	3517094	+	+	+	YPK_3216	conserved in *Y. pestis, Y. pseudotuberculosis*	no
C0217	-	3533525	3533671	++	++	++	YPK_3231	conserved in *Y. pestis, Y. pseudotuberculosis*	no
C0221	-	3579380	3579467	+++	++	++	YPK_3272	conserved in *Y. pestis, Y. pseudotuberculosis*	no
C0223	-	3593486	3593546	+	++	(+)	YPK_3282	conserved in *Y. pestis, Y. pseudotuberculosis*	no
C0224	-	3601523	3601589	+	+	+	YPK_3290	conserved in *Y. pestis, Y. pseudotuberculosis*	no
C0227	+	3661835	3661890	+	+		YPK_3341	conserved in *Y. pestis, Y. pseudotuberculosis*	no
C0229	-	3676629	3676770	+	+++	+	YPK_3349	γ-proteobacteria	no
C0232	+	3679680	3679733	(+)	+	+	YPK_3353	conserved in *Yersinia*	no
C0234	-	3697361	3697465	+		+	YPK_3371	conserved in *Yersinia*	no
C0238	-	3779081	3779158	+	++	(+)	YPK_3445	conserved in *Y. pestis, Y. pseudotuberculosis*	no
C0240	-	3780756	3780832		+		YPK_3446	γ-proteobacteria	no
C0245	+	3816337	3816464	+	+	+	YPK_3474	conserved in *Y. pestis, Y. pseudotuberculosis*	no
C0249	-	3875281	3875333		+	(+)	YPK_3527	conserved in *Y. pestis, Y. pseudotuberculosis*	no
C0256	+	3963630	3963679		++		YPK_3597	conserved in *Y. pestis, Y. pseudotuberculosis*	no
C0257	-	3970528	3970606	+	++	+	YPK_3599	conserved in *Y. pestis, Y. pseudotuberculosis*	no
C0258	-	3979770	3979848	+	+	++	YPK_3607	conserved in *Y. pestis, Y. pseudotuberculosis*	no
C0260	-	3993915	3994003		++		YPK_3619	conserved in *Y. pestis, Y. pseudotuberculosis*	no
C0264	+	4074601	4074650	+		+	YPK_3687	conserved in *Y. pestis, Y. pseudotuberculosis*	no
C0267	-	4118846	4118978	+	+	++	YPK_3727	γ-proteobacteria	S15
C0268	-	4125990	4126094	(+)	++	(+)	YPK_3733	γ-proteobacteria	no
C0269	-	4149640	4149748	+	+	+	YPK_3761	conserved in *Y. pestis, Y. pseudotuberculosis*	no
C0270	-	4155285	4155345	+	+	+	YPK_3768	conserved in *Yersinia*	no
C0272	-	4186637	4186696	+	+		YPK_3799	conserved in *Yersinia*	no
C0276	+	4214489	4214565	+	+	+	YPK_3825	conserved in *Y. pestis, Y. pseudotuberculosis*	no
C0288	-	4530443	4530529	(+)	++++++		YPK_4098	conserved in *Yersinia*	no
C0290	-	4540299	4540572	+	+	+++	YPK_4108	conserved in *Y. pestis, Y. pseudotuberculosis*	no
C0291	+	4545359	4545451		++	+	YPK_4112	conserved in *Y. pestis, Y. pseudotuberculosis*	no
C0295	-	4634560	4634656	+			YPK_4197	conserved in *Y. pestis, Y. pseudotuberculosis*	no
C0297	-	4647484	4647572	++	+	++	YPK_4210	conserved in *Y. pestis, Y. pseudotuberculosis*	no
C0299	-	4688758	4688807	(+)	+		YPK_4249	γ-proteobacteria	no
P0002	+	5772	5863	+	++	+	pYV0006	conserved in *Yersinia*	CopA
P0005	-	20260	20317	+	+	(+)	pYV0024	conserved in *Yersinia*	no
P0008	-	21626	21724	(+)	(+)	+	pYV0026	conserved in *Yersinia*	no

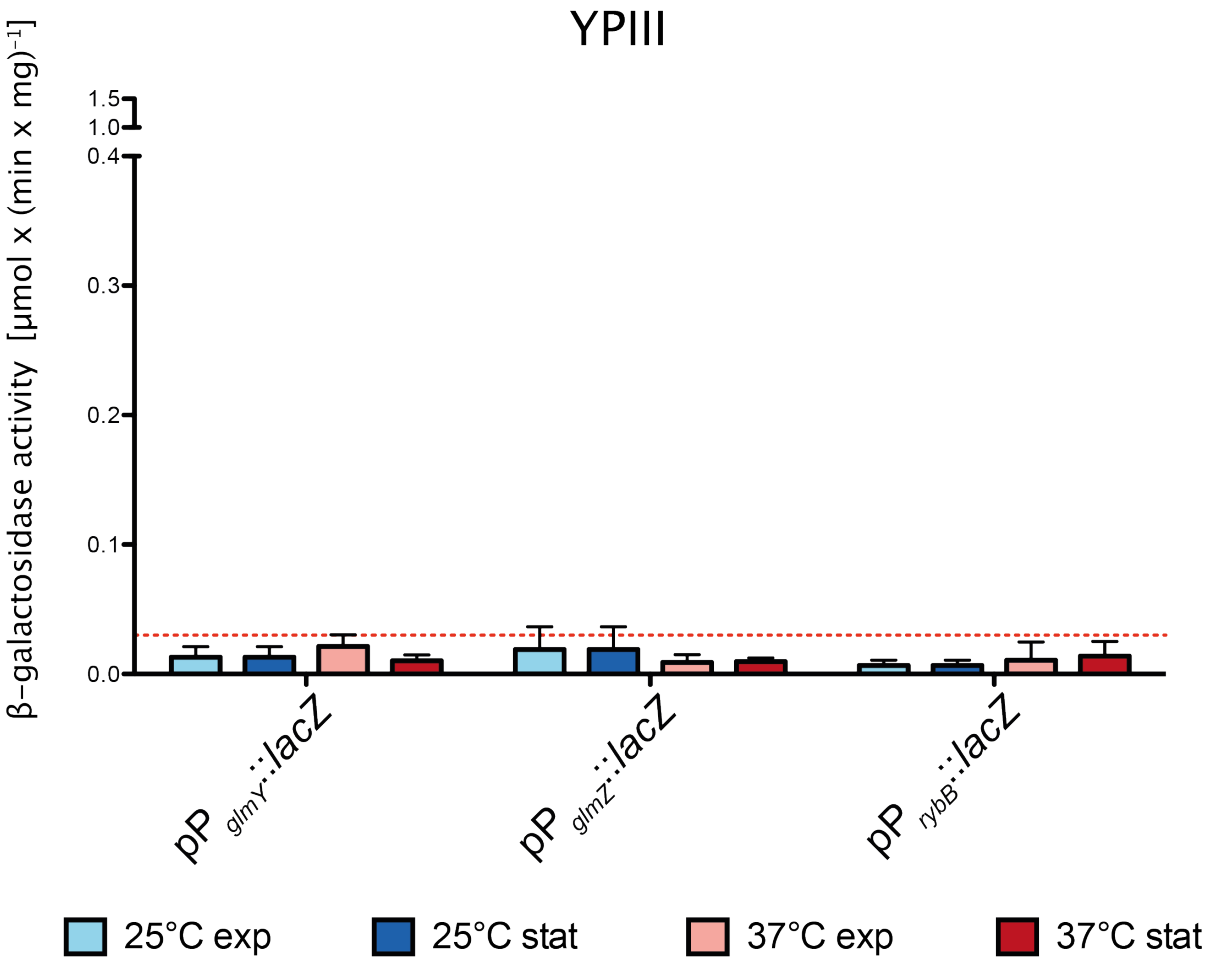

Figure S 1: Expression of the *glmY*-, *glmZ*-, and *rybB-lacZ* reporter constructs in response to temperature and the growth phase. Strains YPIII harboring the respective *lacZ* reporter construct were grown in LB medium at 25°C or 37°C to either exponential or stationary growth. After harvesting, the cells were lysed and the β-galactosidase activity was determined and is given in [µmol x min^{-1} x mg]. The red line indicates the basal activity of the empty vector control**.** The data represent the average and the standard deviation from at least three independent experiments each done in duplicates.

Table S 5: *trans*-encoded sRNAs identified by Illumina Sequencing. The name of the sRNAs is YPK_transRNA_ or YPKp_transRNA_ with running numbers. Inf indicates an infinite upregulation, since no reads were detected in the condition compared to, 0 indicates an infinite downregulation, since no reads were detectable in the second condition. The fold change is only indicated, if it was significant. Therefore, a p-value of 0.05 needed to be present and 30 normalized reads in at least one condition.

ID	Strand	Start	Stop	Length	Gene upstream	Gene downstream	Rfam homology	Sequence homologies	Koo et al., 2011; Beauregard et al., 2013	Fold change 25°C exp to 25°C stat	Fold change 25°C exp to 37°C exp	Fold change wild type to *Δcrp* at 25°C	Fold change wild type to *Δcrp* at 37°C
YPK_transRNA													
1	+	13157	13306	150	YPK_0012	YPK_0013	no	conserved in *Y. pestis*, *Y. pseudotuberculosis*		0.221			1.7
2	-	34173	34277	105	YPK_0030	YPK_0031	no	conserved in *Y. pestis*, *Y. pseudotuberculosis*					
3	+	91812	91863	52	YPK_0079	YPK_0080	no	conserved in *Y. pestis*, *Y. pseudotuberculosis*					
4	-	225461	225663	203	YPK_0173	YPK_0174	no	conserved in *Y. pestis*, *Y. pseudotuberculosis*	Ysr135	9.6			
5	-	374180	374288	109	YPK_0347	YPK_0348	TPP	γ-proteobacteria	Ysr52	2.7			2.9
6	+	494477	494607	131	YPK_0453	YPK_0454	no	conserved in *Y. pestis*, *Y. pseudotuberculosis*	Ysr25	4.1			
7	-	501257	501337	81	YPK_0460	YPK_0461	no	conserved in *Y. pestis*, *Y. pseudotuberculosis*		0.143	0.415	0.111	
8	-	587231	587347	117	YPK_0533	YPK_0534	SraH	conserved in *Y. pestis*, *Y. pseudotuberculosis*		5.7		0.029	0.110
9	+	593906	594284	379	YPK_0540	YPK_0541	RNaseP	γ-proteobacteria	Ysr151	0.441			12.0
10	+	688900	688954	55	YPK_0630	YPK_0631	no	YPIII				3.7	27.8
11	-	699198	699296	99	YPK_0640	YPK_0641	no	*Yersinia*		3.8			2.8
12	-	803749	803811	63	YPK_0742	YPK_0743	no	conserved in *Y. pestis*, *Y. pseudotuberculosis*					Inf
13	+	820766	820824	59	YPK_0745	YPK_0746	no	YPIII					
14	+	826939	827087	149	YPK_0749	YPK_0750	no	*Y. pseudotuberculosis*					0
15	-	984505	984684	180	YPK_0860	YPK_0861	6S	γ-proteo bacteria	Ysr182	21.7		0.493	
16	+	1154464	1154525	62	YPK_1026	YPK_1027	OmrA	*Yersinia*	Ysr149			13.7	
17	-	1158915	1158984	70	YPK_1030	YPK_1031	no	conserved in *Y. pestis*, *Y. pseudotuberculosis*					
18	-	1189068	1189260	193	YPK_1051	YPK_1052	GcvB	γ-proteobacteria	Ysr45/180	0.252		19.3	
19	+	1196489	1196805	317	YPK_1058	YPK_1059	CsrB	γ-proteobacteria	Ysr179	4.6			0.177
20	+	1235814	1236067	254	YPK_1097	YPK_R0085	no	*Yersinia*		0.131	0.369		
21	-	1241697	1241771	75	YPK_R0013	YPK_1101	no	conserved in *Y. pestis*, *Y. pseudotuberculosis*					
22	+	1384237	1384547	311	YPK_1255	YPK_1256	GlmY	*Yersinia*	Ysr147	4.8	0.429		26.5
23	-	1392058	1392223	166	YPK_1263	YPK_1264	no	conserved in *Y. pestis*, *Y. pseudotuberculosis*					0
24	+	1454538	1454696	159	YPK_1324	YPK_1325	no	conserved in *Y. pestis*, *Y. pseudotuberculosis*					
25	-	1454633	1454696	64	YPK_1324	YPK_1325	CyaR	*Yersinia*	Ysr159	14.5		0.002	0.003
26	+	1520743	1520904	162	YPK_1379	YPK_1380	no	conserved in *Y. pestis*, *Y. pseudotuberculosis*	Ysr23	5.4	4.4	10.0	
27	-	1837382	1837464	83	YPK_1654	YPK_1655	no	conserved in *Y. pestis*, *Y. pseudotuberculosis*	Ysr164	8.5	0.077	0.007	0.121
28	-	1928608	1928654	47	YPK_1740	YPK_1741	no	conserved in *Y. pestis*,	Ysr42	8.8			

ID	Strand	Start	Stop	Length	Gene upstream	Gene down-stream	Rfam homo-logy	Sequence homologies	Koo et al., 2011; Beauregard et al., 2013	Fold change 25°C exp to 25°C stat	Fold change 25°C exp to 37°C exp	Fold change wild type to *Δcrp* at 25°C	Fold change wild type to *Δcrp* at 37°C
								Y. pseudo-tuberculosis					
29	+	1931419	1931598	180	YPK_1742	YPK_1743	no	conserved in *Y. pestis*, *Y. pseudo-tuberculosis*		8.2		0.176	0.097
30	-	2017433	2017502	70	YPK_1818	YPK_1819	no	*Yersinia*				10.3	
31	+	2059374	2059597	224	YPK_1853	YPK_1854	no	*Yersinia*					
32	+	2070683	2070762	80	YPK_1862	YPK_1863	no	*Yersinia*	Ysr75				
33	-	2081614	2081873	260	YPK_1875	YPK_1876	no	*Yersinia*					0.091
34	+	2100360	2100499	140	YPK_1892	YPK_1893	RyhB	*Yersinia*	Ysr146		0.063	0.085	0.080
35	+	2161342	2161480	139	YPK_1946	YPK_1947	no	conserved in *Y. pestis*, *Y. pseudo-tuberculosis*		3.3			0.346
36	-	2167074	2167146	73	YPK_1950	YPK_1951	no	conserved in *Y. pestis*, *Y. pseudo-tuberculosis*	sR053	12.6		0.051	0.045
37	-	2289465	2289603	139	YPK_2061	YPK_2062	no	conserved in *Y. pestis*, *Y. pseudo-tuberculosis*			0.470	0.188	
38	-	2310065	2310374	310	YPK_2078	YPK_2079	no	conserved in *Y. pestis*, *Y. pseudo-tuberculosis*				186.1	40.5
39	+	2357330	2357483	154	YPK_2125	YPK_2126	no	conserved in *Y. pestis*, *Y. pseudo-tuberculosis*	Ysr16	12.2			
40	-	2362741	2363026	286	YPK_2131	YPK_2132	no	γ-proteo-bacteria	Ysr72	3.7		0.222	
41	-	2564181	2564329	149	YPK_2324	YPK_2325	no	*Y. pseudo-tuberculosis*	Ysr70				
42	-	2587385	2587430	46	YPK_R0072	YPK_2354	no	*Yersinia*				0.243	0.266
43	-	2636874	2636965	92	YPK_2404	YPK_2405	no	*Y. pseudo-tuberculosis*					
44	-	2668705	2668852	148	YPK_2434	YPK_2435	SraC	γ-proteo-bacteria	+	74.0			
45	+	2670912	2671000	89	YPK_2437	YPK_2438	no	conserved in *Y. pestis*, *Y. pseudo-tuberculosis*					0.142
46	-	2756285	2757506	1222	YPK_2516	YPK_2517	CRISPR-DR4	YPIII		8.1			1.8
47	-	2757738	2758104	367	YPK_2516	YPK_2517	CRISPR-DR4	YPIII		16.3		0.248	
48	+	2766343	2766478	136	YPK_2524	YPK_2525	no	*Yersinia*			0.346	0.306	
49	-	2811349	2811396	48	YPK_2561	YPK_2562	no	*Yersinia*					
50	-	2892626	2892900	275	YPK_2636	YPK_2637	no	γ-proteo-bacteria		1278.3		0.063	
51	+	2926425	2926704	280	YPK_2659	YPK_2660	no	conserved in *Y. pestis*, *Y. pseudo-tuberculosis*		3.2			
52	+	2971735	2971907	173	YPK_2691	YPK_2692	no	conserved in *Y. pestis*, *Y. pseudo-tuberculosis*	Ysr65	4.1			
53	+	3015956	3016048	93	YPK_2734	YPK_2735	RybB	γ-proteo-bacteria		62.2	5.1	0.122	2.7
54	+	3119604	3119664	61	YPK_2834	YPK_2835	no	conserved in *Y. pestis*, *Y. pseudo-tuberculosis*	Ysr62	50.2		0.002	0
55	+	3184715	3184773	59	YPK_2887	YPK_2888	no	conserved in *Y. pestis*, *Y. pseudo-tuberculosis*					0
56	+	3262357	3262518	162	YPK_2964	YPK_2965	no	conserved in *Y. pestis*, *Y. pseudo-tuberculosis*		7.2		0.148	
57	+	3279865	3280284	420	YPK_2980	YPK_2981	ssrA	γ-proteo-bacteria	+	6.0			4.5
58	+	3311298	3311500	203	YPK_3009	YPK_3010	no	conserved in *Y. pestis*, *Y. pseudo-tuberculosis*		3.3	9		
59	+	3407357	3407451	95	YPK_3109	YPK_3110	no	YPIII		130.7			
60	-	3463932	3464026	95	YPK_3166	YPK_3167	MicM	conserved in *Y. pestis*, *Y. pseudo-tuberculosis*	Ysr145			63.9	22.8
61	-	3515601	3515708	108	YPK_3214	YPK_3215	SRP	γ-proteo-bacteria	+	2.6			3.8
62	+	3597123	3597181	59	YPK_3286	YPK_3287	no	conserved in *Y. pestis*, *Y. pseudo-*				8.6	

ID	Strand	Start	Stop	Length	Gene upstream	Gene down-stream	Rfam homo-logy	Sequence homologies	Koo et al., 2011; Beauregard et al., 2013	Fold change 25°C exp to 25°C stat	Fold change 25°C exp to 37°C exp	Fold change wild type to *Δcrp* at 25°C	Fold change wild type to *Δcrp* at 37°C
								tuberculosis					
63	-	3673750	3673813	64	YPK_R0091	YPK_3349	no	*Yersinia*					
64	-	3676684	3676769	86	YPK_3349	YPK_3350	no	conserved in *Y. pestis*, *Y. pseudo-tuberculosis*			3.3		11.6
65	+	3694598	3694667	70	YPK_3368	YPK_3369	MicA	γ-proteo-bacteria	Ysr7/154	10.5	7.8	4.2	19.6
66	-	3698246	3698331	86	YPK_R0054	YPK_3372	no	γ-proteo-bacteria				0.049	0.202
67	+	3698437	3698529	93	YPK_R0054	YPK_3372	no	conserved in *Y. pestis*, *Y. pseudo-tuberculosis*	Ysr59, sR034		5.4		
68	-	3716921	3717244	324	YPK_3387	YPK_3388	no	conserved in *Y. pestis*, *Y. pseudo-tuberculosis*	Ysr110, sR065				0,262
69	-	3853114	3853166	53	YPK_3508	YPK_3509	no	conserved in *Y. pestis*, *Y. pseudo-tuberculosis*					
70	+	3885443	3885564	122	YPK_3534	YPK_3535	Leu leader	γ-proteo-bacteria					
71	+	4005578	4005629	52	YPK_3628	YPK_3629	no	conserved in *Y. pestis*, *Y. pseudo-tuberculosis*					
72	-	4023719	4023831	113	YPK_3644	YPK_3645	no	conserved in *Y. pestis*, *Y. pseudo-tuberculosis*		59.3		0.192	
73	-	4072818	4072925	108	YPK_3685	YPK_3686	no	conserved in *Y. pestis*, *Y. pseudo-tuberculosis*	Ysr103	10.6			0.079
74	-	4249444	4249563	120	YPK_3856	YPK_3857	no	conserved in *Y. pestis*, *Y. pseudo-tuberculosis*	Ysr100	2.4		0.191	0.268
75	-	4432519	4432735	217	YPK_4019	YPK_R0045	GlmZ	*Yersinia*	Ysr148	3.6			
76	-	4435525	4435649	125	YPK_4021	YPK_4022	no	conserved in *Y. pestis*, *Y. pseudo-tuberculosis*					
77	-	4601525	4601805	281	YPK_4173	YPK_4174	no	conserved in *Y. pestis*, *Y. pseudo-tuberculosis*		13.0		0.206	
78	+	4619059	4619182	124	YPK_4187	YPK_4188	no	conserved in *Y. pestis*, *Y. pseudo-tuberculosis*	Ysr1			0.272	
79	+	4623011	4623073	63	YPK_4189	YPK_4190	no	conserved in *Y. pestis*, *Y. pseudo-tuberculosis*	Ysr49				
80	-	4628088	4628384	297	YPK_4193	YPK_4194	CsrC	*Yersinia*	Ysr186	7.4	2.1	0.019	0.047
81	-	4629466	4629551	86	YPK_4194	YPK_4195	Spot42	γ-proteo-bacteria	Ysr185			29.0	
YPKp_transRNA													
1	+	16567	16636	70	pYV0019	pYV0020	no	conserved in *Y. pestis*, *Y. pseudo-tuberculosis*					
2	-	36081	36125	45	pYV0052	pYV0053	no	*Yersinia*					

Table S 6: antisense-encoded sRNAs identified by Illumina sequencing. The name of the sRNAs is YPK_asRNA_ or YPKp_asRNA_ with running numbers. Inf indicates an infinite upregulation, since no reads were detected in the condition compared to, 0 indicates an infinite downregulation, since no reads were detectable in the second condition. The fold change is only indicated, if it was significant. Therefore, a p-value of 0.05 needed to be present and 30 normalized reads in at least one condition.

ID	strand	start	stop	length	antisense feature	Rfam homology	Sequence homology	fold change 25°C exp to 25°C stat	fold change 25°C exp to 37°C exp	fold change wild type to *Δcrp* at 25°C	fold change wild type to *Δcrp* at 37°C
YPK_asRNA											
1	-	28064	28250	187	YPK_0024	no	conserved in *Y. pestis*, *Y. pseudo-tuberculosis*		2.2		
2	+	252843	253006	164	YPK_0215, YPK_0216	no	YPIII	9.9			
3	-	328669	329005	337	YPK_0303	no	γ-proteo-bacteria			4.9	
4	-	417549	418381	833	YPK_0382, YPK_0383	no	*Yersinia*	3.9		29.7	
5	+	518362	518465	104	YPK_0473	no	YPIII				0
6	-	684722	684998	277	YPK_0623, YPK_0624	no	YPIII				0
7	-	838097	838150	54	YPK_0751	no	conserved in *Y. pestis*, *Y. pseudo-tuberculosis*				
8	+	898356	898599	244	YPK_0790	no	conserved in *Y. pestis*, *Y. pseudo-tuberculosis*				
9	+	1333749	1333796	48	YPK_1198	no	YPIII				
10	+	1441743	1441800	58	YPK_1315	no	YPIII				0.148
11	-	1548755	1548954	200	YPK_1405	no	γ-proteo-bacteria				
12	-	1649603	1649650	48	YPK_1486	no	conserved in *Y. pestis*, *Y. pseudo-tuberculosis*	2.3			0.266
13	-	1715585	1715818	234	YPK_1552	no	conserved in *Y. pestis*, *Y. pseudo-tuberculosis*				
14	+	1785857	1785981	125	YPK_1614	no	conserved in *Y. pestis*, *Y. pseudo-tuberculosis*	3.4		0.178	0.067
15	+	1840773	1840868	96	YPK_1658	no	*Y. pseudo-tuberculosis*				0.066
16	-	2015932	2016053	122	YPK_1816	no	conserved in *Y. pestis*, *Y. pseudo-tuberculosis*	15.5			
17	-	2029876	2029925	50	YPK_1831	no	conserved in *Y. pestis*, *Y. pseudo-tuberculosis*				0
18	+	2111544	2111719	176	YPK_1905	no	conserved in *Y. pestis*, *Y. pseudo-tuberculosis*				0.199
19	+	2139280	2139558	279	YPK_1928	no	γ-proteo-bacteria				0
20	-	2234751	2234922	172	YPK_2007	no	conserved in *Y. pestis*, *Y. pseudo-tuberculosis*				0
21	+	2237657	2237719	63	YPK_2009	no	conserved in *Y. pestis*, *Y. pseudo-tuberculosis*	4.9		0.036	
22	-	2289852	2289941	90	YPK_2062	no	conserved in *Y. pestis*, *Y. pseudo-tuberculosis*				
23	+	2473453	2473632	180	YPK_2230, YPK_2231	no	conserved in *Y. pestis*, *Y. pseudo-tuberculosis*	3.3		0.191	0.155
24	+	2479654	2479909	256	YPK_2235	no	*Yersinia*				
25	+	2610124	2610197	74	YPK_2375	no	conserved in *Y. pestis*, *Y. pseudo-tuberculosis*			0.160	
26	-	2700872	2701618	747	YPK_2467, YPK_2468	no	*Yersinia*	13.1			0.349
27	-	2764335	2764535	201	YPK_2521, YPK_2522,	no	conserved in *Y. pestis*,	5.5			

ID	strand	start	stop	length	antisense feature	Rfam homology	Sequence homology	fold change 25°C exp to 25°C stat	fold change 25°C exp to 37°C exp	fold change wild type to *Δcrp* at 25°C	fold change wild type to *Δcrp* at 37°C
					YPK_2523		*Y. pseudo-tuberculosis*				
28	+	2857343	2857392	50	YPK_2601	no	conserved in *Y. pestis*, *Y. pseudo-tuberculosis*				
29	-	2867525	2867702	178	YPK_2614	no	conserved in *Y. pestis*, *Y. pseudo-tuberculosis*				0.046
30	-	2966053	2966663	611	YPK_2687	no	conserved in *Y. pestis*, *Y. pseudo-tuberculosis*	5.5		17.9	
31	-	2975155	2975300	146	YPK_2694	no	conserved in *Y. pestis*, *Y. pseudo-tuberculosis*				
32	-	2984438	2984498	61	YPK_2701	no	conserved in *Y. pestis*, *Y. pseudo-tuberculosis*				0
33	-	3074143	3074282	140	YPK_2785	no	conserved in *Y. pestis*, *Y. pseudo-tuberculosis*	Inf			0
34	-	3399141	3399237	97	YPK_3095	no	YPIII				
35	+	3399634	3399711	78	YPK_3096	no	YPIII				
36	-	3403622	3403696	75	YPK_3103	no	YPIII	0.090	0.250		
37	+	3426074	3426192	119	YPK_3132, YPK_3133	no	YPIII				
38	-	3464893	3465133	241	YPK_3168, YPK_3169	no	conserved in *Y. pestis*, *Y. pseudo-tuberculosis*				0.166
39	+	3567635	3567691	57	YPK_3262	no	conserved in *Y. pestis*, *Y. pseudo-tuberculosis*				
40	+	3593022	3593098	77	YPK_3282	no	conserved in *Y. pestis*, *Y. pseudo-tuberculosis*				
41	-	3603859	3604044	186	YPK_3293	no	conserved in *Y. pestis*, *Y. pseudo-tuberculosis*				
42	+	3636213	3636267	55	YPK_3314	no	conserved in *Y. pestis*, *Y. pseudo-tuberculosis*				
43	-	3678968	3679169	202	YPK_3352	no	γ-proteo-bacteria	2.6		0.285	
44	+	3680138	3680213	76	YPK_3354	no	conserved in *Y. pestis*, *Y. pseudo-tuberculosis*				
45	-	3856677	3856812	136	YPK_3511	no	conserved in *Y. pestis*, *Y. pseudo-tuberculosis*				
46	-	3856989	3857210	222	YPK_3511	no	conserved in *Y. pestis*, *Y. pseudo-tuberculosis*		0,683	2,694	2,4
47	+	3879774	3879836	63	YPK_3531	no	conserved in *Y. pestis*, *Y. pseudo-tuberculosis*				
48	-	3981783	3981933	151	YPK_3611	no	*Yersinia*			0,029	
49	-	3987977	3988291	315	YPK_3614	no	conserved in *Y. pestis*, *Y. pseudo-tuberculosis*	7.4		0.412	0.270
50	-	4040928	4041008	81	YPK_3658	no	conserved in *Y. pestis*, *Y. pseudo-tuberculosis*				
51	+	4061730	4061839	110	YPK_3677	no	conserved in *Y. pestis*, *Y. pseudo-tuberculosis*				
52	-	4064418	4064612	195	YPK_3679	no	γ-proteo-bacteria		2.2		
53	+	4114840	4115091	252	YPK_3724	no	γ-proteo-bacteria	4.8		0.202	
54	-	4131381	4131674	294	YPK_3738	no	*Yersinia*		0.184		
55	-	4209089	4209167	79	YPK_3819	no	conserved in *Y. pestis*, *Y. pseudo-tuberculosis*				

ID	strand	start	stop	length	antisense feature	Rfam homology	Sequence homology	fold change 25°C exp to 25°C stat	fold change 25°C exp to 37°C exp	fold change wild type to *Δcrp* at 25°C	fold change wild type to *Δcrp* at 37°C
56	+	4210857	4210958	102	YPK_3821	no	conserved in *Y. pestis*, *Y. pseudo-tuberculosis*	41.1		0.052	
57	-	4414984	4415039	56	YPK_4003	no	γ-proteo-bacteria	0.209	0.206		
58	+	4496352	4496424	73	YPK_4072	no	conserved in *Y. pestis*, *Y. pseudo-tuberculosis*				
59	-	4556153	4556405	253	YPK_4122	no	conserved in *Y. pestis*, *Y. pseudo-tuberculosis*				
60	+	4576414	4576471	58	YPK_4144	no	conserved in *Y. pestis*, *Y. pseudo-tuberculosis*		0.227		
61	-	4596983	4597168	186	YPK_4167	no	γ-proteo-bacteria				
YPKp_asRNA											
1	+	181	358	178	pYV0001	no	*Yersinia*	2.3			
2	+	1213	1450	238	pYV0001	no	*Yersinia*				
3	+	1766	1840	75	pYV0001	no	*Yersinia*	15.6			2.0
4	+	17413	17560	148	pYV0021	no	γ-proteo-bacteria				
5	+	19070	19139	70	pYV0022	no	γ-proteo-bacteria			30.3	22.9
6	-	31549	31659	111	pYV0043, pYV0044	no	*Yersinia*				
7	+	36602	36654	53	pYV0054	no	*Yersinia*				
8	+	39187	39466	280	pYV0056, pYV0057	no	*Yersinia*				
9	+	39960	40082	123	pYV0057, pYV0058	no	*Yersinia*				0.200
10	+	41789	41893	105	pYV0060	no	*Yersinia*				
11	-	47755	47835	81	pYV0069	no	*Yersinia*	2,5			
12	-	49011	49074	64	pYV0070	no	*Yersinia*				
13	-	50419	50548	130	pYV0072, pYV0073	no	*Yersinia*				
14	-	53075	53361	287	pYV0075	no	*Yersinia*				0,270
15	-	54369	54449	81	pYV0078	no	*Yersinia*				
16	-	55893	56043	151	pYV0079	no	*Yersinia*				
17	-	57338	57391	54	pYV0080	no	*Yersinia*				
18	-	59480	59767	288	pYV0085, pYV0086	no	*Yersinia*	6.7			
19	-	60948	61048	101	pYV0087	no	*Yersinia*				4.4

Table S 7: Genes that were differentially regulated in a growth phase-dependent manner.

The fold change is indicated for the condition in which the gene expression was upregulated.

Locus	Gene name	Gene description	Condition upregulated	Fold change	p-value
Virulence					
pYV0060	*lcrD, yscV*	putative membrane-bound Yop protein	YPIII_E25	**2,3**	4,8E-04
pYV0079	*yscC*	putative type III secretion protein	YPIII_E25	**2,2**	7,2E-03
pYV0080	*yscD*	putative type III secretion protein	YPIII_E25	**2,9**	4,3E-03
pYV0081	*yscE*	putative type III secretion protein	YPIII_E25	**5,7**	1,6E-06
pYV0082	*yscF*	putative type III secretion protein	YPIII_E25	**2,4**	3,1E-03
pYV0087	*yscK*	putative type III secretion protein	YPIII_E25	**2,2**	6,4E-03
YPK_1606	*ompX/ailD*	virulence-related outer membrane protein	YPIII_E25	**16,0**	1,4E-06
YPK_1953	*srfB*	putative virulence factor SrfB	YPIII_E25	**20,9**	3,5E-19
pYV0020	*sycH*	putative yopH targeting protein	YPIII_S25	**3,0**	1,0E-04
pYV0058	*lcrG*	putative Yop regulator	YPIII_S25	**2,6**	1,4E-03
pYV0075	*virG*	putative Yop targeting lipoprotein	YPIII_S25	**3,3**	3,3E-03
pYV0076	*lcrF, virF*	putative thermoregulatory protein	YPIII_S25	**6,7**	1,2E-05
pYV0077	*yscA*	type III secretion protein YscA	YPIII_S25	**2,2**	1,6E-02
pYV0089	*yscM, lcrQ*	putative type III secretion regulatory	YPIII_S25	**3,6**	4,0E-03
pYV0094	*yopH*	putative protein-tyrosine phosphatase Yop effector	YPIII_S25	**3,4**	3,7E-07
YPK_0052	*yqiG*	fimbrial biogenesis outer membrane usher protein	YPIII_S25	**4,5**	4,1E-02
YPK_0053	*fimC-1*	pili assembly chaperone	YPIII_S25		8,3E-03
YPK_0280	*bfd*	BFD domain protein (2Fe-2S)-binding domain protein	YPIII_S25	**3,9**	5,1E-07
YPK_0281	*bfr*	bacterioferritin	YPIII_S25	**86,6**	1,8E-13
YPK_0445	*pcp*	17 kDa surface antigen	YPIII_S25	**3,0**	1,1E-02
YPK_0575	*fhaB-3*	putative adhesin	YPIII_S25	**2,7**	1,6E-02
YPK_0695		fimbrial biogenesis outer membrane usher protein	YPIII_S25	**11,2**	2,8E-13
YPK_0696	*papD*	pili assembly chaperone	YPIII_S25	**24,8**	4,9E-14
YPK_0697		fimbrial protein	YPIII_S25	**27,8**	1,8E-11
YPK_0736	*slyB-1*	17 kDa surface antigen	YPIII_S25	**2,2**	4,6E-02
YPK_0764	*vgrG*	type VI secretion system Vgr family protein	YPIII_S25	**6,0**	2,9E-02
YPK_0871	*yadF*	YadA domain protein	YPIII_S25	**2,6**	8,7E-03
YPK_0873	*yqfA, hlyIII*	channel protein, hemolysin III family	YPIII_S25	**2,7**	2,7E-02
YPK_1315	*yeeJ*	Ig domain protein group 1 domain protein	YPIII_S25	**6,2**	2,8E-05

Locus	Gene name	Gene description	Condition upregulated	Fold change	p-value
YPK_1473	*impG, vasA*	type VI secretion protein, VC_A0110 family	YPIII_S25	**24,2**	1,0E-02
YPK_1485	*impL, vasK, icmF*	type VI secretion protein IcmF	YPIII_S25	**7,4**	1,4E-03
YPK_1486		type VI secretion system Vgr family protein	YPIII_S25	**3,8**	2,4E-04
YPK_1489	*impE*	virulence protein SciE type	YPIII_S25	**3,5**	2,0E-02
YPK_1490	*impF*	type VI secretion system lysozyme-related protein	YPIII_S25	**10,8**	3,1E-04
YPK_1559	*rovM*	transcriptional regulator, LysR family	YPIII_S25	**13,7**	3,6E-11
YPK_1655	*ypsR*	transcriptional regulator, LuxR family	YPIII_S25	**2,3**	4,4E-02
YPK_1705	*ycfJ*	17 kDa surface antigen	YPIII_S25	**10,4**	1,3E-10
YPK_1761	*yadE*	YadA domain protein	YPIII_S25	**17,1**	1,8E-12
YPK_1774	*fimD, fimC, mrkC, htrE, cssD*	fimbrial biogenesis outer membrane usher protein	YPIII_S25	**7,6**	2,5E-02
YPK_1775	*fimC-2*	chaperone protein	YPIII_S25	**23,3**	2,5E-02
YPK_1786	*fimA-3*	fimbrial protein	YPIII_S25	**20,6**	3,3E-13
YPK_1787	*ecpD*	pili assembly chaperone	YPIII_S25	**31,0**	4,2E-04
YPK_1789	*fimA-4*	Fimbrial protein	YPIII_S25	**3,9**	1,4E-02
YPK_1876	*rovA*	transcriptional regulator, MarR family	YPIII_S25	**2,8**	1,8E-05
YPK_2156	*hlyA*	filamentous haemagglutinin domain protein	YPIII_S25	**5,7**	4,9E-07
YPK_2429	*invA*	invasin region 3	YPIII_S25	**4,6**	1,4E-10
YPK_2513	*invB/ifp*	Ig domain protein group 1 domain protein	YPIII_S25	**3,6**	3,0E-03
YPK_2757	*psaC*	fimbrial biogenesis outer membrane usher protein	YPIII_S25	**4,7**	5,7E-04
YPK_2758	*psaB*	pili assembly chaperone	YPIII_S25		2,0E-10
YPK_2759	*psaA*	pH 6 antigen precursor (antigen 4) (adhesin)	YPIII_S25	**94,3**	2,7E-24
YPK_2760	*psaF*	conserved hypothetical protein	YPIII_S25	**35,6**	8,0E-14
YPK_2761	*psaE*	transcriptional regulator, CadC	YPIII_S25	**68,0**	1,8E-24
YPK_2900	*ybhG, yhiI*	secretion protein HlyD family protein	YPIII_S25	**3,8**	1,7E-02
YPK_3289	*crl*	transcriptional regulator Crl	YPIII_S25	**2,3**	4,1E-03
YPK_3408	*yahD, arpA*	ShET2 enterotoxin domain protein	YPIII_S25	**3,2**	2,2E-02
YPK_3561	*impG-2, vasA-2*	type VI secretion protein, VC_A0110 family	YPIII_S25	**7,9**	2,6E-03
YPK_3563	*impC-2*	protein of unknown function DUF796	YPIII_S25	**7,9**	8,2E-13
YPK_3564	*impC-3*	type VI secretion protein, EvpB/VC_A0108 family	YPIII_S25	**4,7**	3,3E-03
YPK_3653	*lsrB*	autoinducer AI-2 ABC transporter, periplasmic AI-2-binding protein	YPIII_S25	**29,1**	5,2E-05
YPK_4085	*HasA*	heme-binding A family protein	YPIII_S25	**3,5**	2,6E-02
Cell motility and chemotaxis					
YPK_0034	*tar*	methyl-accepting chemotaxis sensory transducer	YPIII_E25	**5,7**	5,7E-06
YPK_1748	*motB*	OmpA/MotB domain protein	YPIII_E25	**2,2**	1,8E-03
YPK_1749	*cheA*	CheA signal transduction histidine kinase	YPIII_E25	**4,0**	7,8E-08
YPK_1750	*cheW*	CheW protein	YPIII_E25	**4,3**	4,9E-05
YPK_1753	*cheD*	methyl-accepting chemotaxis sensory transducer	YPIII_E25	**15,3**	1,8E-17
YPK_1756	*cheR*	MCP methyltransferase, CheR-type	YPIII_E25	**94,2**	1,7E-11
YPK_1757	*cheB*	response regulator receiver modulated CheB methylesterase	YPIII_E25	**11,3**	1,6E-08
YPK_1758	*cheY*	response regulator receiver protein	YPIII_E25	**11,3**	2,3E-06
YPK_1759	*cheZ*	chemotaxis phosphatase, CheZ	YPIII_E25	**6,3**	6,4E-07
YPK_2378	*fliZ*	flagella biosynthesis protein FliZ	YPIII_E25	**10,5**	1,6E-11
YPK_2380	*fliA*	RNA polymerase, sigma 28 subunit, FliA/WhiG	YPIII_E25	**22,4**	9,7E-20
YPK_2381	*fliC*	flagellin domain protein	YPIII_E25	**39,3**	1,3E-36
YPK_2382	*fliD*	flagellar hook-associated 2 domain protein	YPIII_E25	**13,6**	7,0E-18
YPK_2383	*fliS*	flagellar protein FliS	YPIII_E25	**13,2**	2,6E-11
YPK_2384	*fliT*	flagellar export chaperone	YPIII_E25	**8,3**	1,8E-06
YPK_2390	*fliE*	flagellar hook-basal body complex subunit FliE	YPIII_E25	**43,3**	9,0E-10
YPK_2391	*fliF*	flagellar M-ring protein FliF	YPIII_E25	**44,4**	1,2E-25
YPK_2392	*fliG*	flagellar motor switch protein FliG	YPIII_E25	**32,0**	2,4E-19
YPK_2393	*fliH*	flagellar assembly protein FliH	YPIII_E25	**94,1**	1,8E-14
YPK_2394	*fliI*	ATPase, FliI/YscN family	YPIII_E25	**69,1**	1,9E-16
YPK_2395	*fliJ*	flagellar export protein FliJ	YPIII_E25	**90,5**	3,9E-11
YPK_2396	*fliK-1*	flagellar hook-length control protein	YPIII_E25	**85,5**	2,0E-11
YPK_2398	*fliL*	flagellar basal body-associated protein FliL	YPIII_E25	**20,3**	2,8E-17
YPK_2399	*fliM*	flagellar motor switch protein FliM	YPIII_E25	**71,2**	2,9E-25
YPK_2400	*fliN*	flagellar motor switch protein FliN	YPIII_E25	**37,4**	5,2E-15
YPK_2401	*fliO*	flagellar biosynthesis protein FliO	YPIII_E25	**54,7**	1,9E-14
YPK_2402	*fliP*	flagellar biosynthetic protein FliP	YPIII_E25		5,7E-15
YPK_2403	*fliQ*	flagellar biosynthetic protein FliQ	YPIII_E25		7,1E-04
YPK_2404	*fliR*	flagellar biosynthetic protein FliR	YPIII_E25		3,7E-05
YPK_2415	*flgL*	flagellar hook-associated protein 3	YPIII_E25	**25,8**	7,7E-20
YPK_2416	*flgK*	flagellar hook-associated protein FlgK	YPIII_E25	**39,5**	1,5E-22
YPK_2417	*flgJ*	flagellar rod assembly protein/muramidase FlgJ	YPIII_E25	**91,6**	4,2E-14
YPK_2418	*flgI*	flagellar P-ring protein	YPIII_E25	**58,8**	1,0E-13
YPK_2419	*flgH*	flagellar L-ring protein	YPIII_E25	**77,1**	7,7E-16
YPK_2420	*flgG*	flagellar basal-body rod protein FlgG	YPIII_E25	**58,4**	7,7E-24
YPK_2421	*flgF*	flagellar basal-body rod protein FlgF	YPIII_E25	**49,1**	2,0E-22
YPK_2422	*flgE*	flagellar basal body FlaE domain protein	YPIII_E25	**1079,7**	5,0E-44
YPK_2423	*flgD*	flagellar hook capping protein	YPIII_E25	**102,8**	1,5E-28
YPK_2424	*flgC*	flagellar basal-body rod protein FlgC	YPIII_E25	**292,2**	2,7E-24
YPK_2425	*flgB*	flagellar basal-body rod protein FlgB	YPIII_E25	**57,1**	1,1E-27
YPK_2426	*flgA*	flagella basal body P-ring formation protein FlgA	YPIII_E25	**26,4**	5,2E-12
YPK_2427	*flgM*	anti-sigma-28 factor, FlgM	YPIII_E25	**2,8**	1,3E-03
YPK_2428	*flgN*	FlgN family protein	YPIII_E25	**12,1**	4,9E-11
YPK_2430	*flhE*	flagellar FlhE family protein	YPIII_E25	**5,9**	2,7E-02
YPK_2431	*flhA*	flagellar biosynthesis protein FlhA	YPIII_E25	**8,5**	2,7E-10
YPK_2432	*flhB*	flagellar biosynthetic protein FlhB	YPIII_E25	**19,8**	5,9E-12
YPK_2833	*tsr2*	methyl-accepting chemotaxis sensory transducer with Cache sensor	YPIII_E25	**2,6**	1,6E-02
YPK_0479		insecticidal toxin complex protein	YPIII_S25	**9,3**	3,9E-03
YPK_1018	*cheD*	methyl-accepting chemotaxis sensory transducer	YPIII_S25	**20,1**	1,5E-03
YPK_1037	*ppdA*	prepilin peptidase dependent protein A	YPIII_S25	**23,4**	1,8E-12
YPK_1348	*fliB*	protein of unknown function UPF0153	YPIII_S25	**3,5**	5,1E-03
YPK_1597	*mcp*	Pas/Pac sensor-containing methyl-accepting chemotaxis sensory transducer	YPIII_S25	**6,2**	1,0E-02
YPK_1745	*flhD*	flagellar transcriptional activator	YPIII_S25	**2,2**	4,1E-04
Stress adaptation					
YPK_0011	*ibpA*	heat shock protein Hsp20	YPIII_E25	**2,4**	3,3E-02
YPK_0012	*ibpB*	heat shock protein Hsp20	YPIII_E25	**2,8**	3,4E-02
YPK_0175	*hslO*	Hsp33 protein	YPIII_E25	**8,0**	2,1E-09
YPK_0444	*cspA-3*	cold-shock DNA-binding domain protein	YPIII_E25	**6,8**	1,4E-02
YPK_0526	*sspA*	glutathione S-transferase domain	YPIII_E25	**3,2**	4,4E-06

Locus	Gene name	Gene description	Condition upregulated	Fold change	p-value
YPK_0838	*gshB*	glutathione synthetase	YPIII_E25	**2,4**	3,0E-03
YPK_1124	*cspB-1*	cold-shock DNA-binding domain protein	YPIII_E25	**4,9**	1,9E-02
YPK_1740	*cspC-1*	cold-shock DNA-binding domain protein	YPIII_E25	**132,2**	7,4E-19
YPK_2662	*cspB-2*	cold-shock DNA-binding domain protein	YPIII_E25	**6,9**	4,3E-06
YPK_2830	*msgA*	DinI family protein; putative stress response protein	YPIII_E25	**2,3**	4,5E-02
YPK_3161	*ybbN*	thioredoxin domain	YPIII_E25	**3,8**	1,5E-05
YPK_3195	*htpG*	heat shock protein Hsp90	YPIII_E25	**16,1**	1,0E-21
YPK_3445	*sodC*	superoxide dismutase	YPIII_E25	**2,1**	1,2E-02
YPK_3822	*groEL*	chaperonin GroEL	YPIII_E25	**7,6**	2,3E-14
YPK_3823	*groES*	chaperonin Cpn10	YPIII_E25	**6,5**	2,9E-12
YPK_3872	*terE*	stress protein	YPIII_E25	**2,5**	5,0E-03
YPK_3873	*terD*	stress protein	YPIII_E25	**5,3**	5,5E-07
YPK_3874	*terC*	integral membrane protein TerC	YPIII_E25	**2,7**	3,7E-04
YPK_3875	*terB*	tellurite resistance TerB	YPIII_E25	**4,7**	3,8E-06
YPK_3876	*terA*	stress protein	YPIII_E25	**9,6**	1,5E-10
YPK_3877	*terZ*	stress protein	YPIII_E25	**5,8**	1,3E-06
YPK_4080		glutaredoxin-family domain protein	YPIII_E25	**2,3**	1,6E-02
YPK_4103	*hslV*	20S proteasome A and B subunits	YPIII_E25	**18,1**	2,2E-14
YPK_4104	*hslU*	heat shock protein HslVU, ATPase subunit HslU	YPIII_E25	**8,2**	1,2E-12
YPK_0120	*uspA*	UspA domain protein	YPIII_S25	**47,6**	3,2E-43
YPK_0121	*uspB*	universal stress protein B	YPIII_S25	**116,9**	9,5E-14
YPK_0437	*yghU*	glutathione S-transferase domain	YPIII_S25	**5,7**	1,2E-09
YPK_0543	*yqjG*	putative glutathione S-transferase	YPIII_S25	**9,4**	3,0E-05
YPK_0564	*hdeD*	acid-resistance membrane protein	YPIII_S25	**6,7**	3,6E-13
YPK_0569	*terX*	stress protein	YPIII_S25	**5,7**	5,3E-03
YPK_1120		acid shock repeat protein	YPIII_S25	**7,0**	3,3E-02
YPK_1140	*hdeB*	acid-resistance protein	YPIII_S25	**6,7**	1,7E-11
YPK_1602	*dps*	ferritin Dps family protein	YPIII_S25	**25,0**	2,4E-31
YPK_1863	*sodB*	superoxide dismutase	YPIII_S25	**17,4**	9,1E-19
YPK_1883	*gst*	glutathione S-transferase domain	YPIII_S25	**7,3**	2,9E-13
YPK_1895	*pspB*	phage shock protein B	YPIII_S25	**3,9**	4,4E-02
YPK_1917	*hslJ*	heat-inducible protein	YPIII_S25	**2,4**	1,1E-03
YPK_1929		acid shock protein	YPIII_S25	**6,6**	1,1E-04
YPK_1943	*uspE*	UspA domain protein	YPIII_S25	**25,2**	1,8E-31
YPK_2017	*cstA-1*	carbon starvation protein CstA	YPIII_S25	**9,2**	3,5E-12
YPK_2355	*uvrC*	excinuclease ABC, C subunit	YPIII_S25	**2,7**	2,4E-04
YPK_2694	*cspD-2*	cold-shock DNA-binding domain protein	YPIII_S25	**104,8**	3,0E-25
YPK_2747	*yliJ, gst*	glutathione S-transferase domain	YPIII_S25	**7,8**	1,3E-08
YPK_2855	*katA*	catalase	YPIII_S25	**37,8**	1,8E-29
YPK_3031	*cspE*	cold-shock DNA-binding domain protein	YPIII_S25	**25,9**	2,0E-12
YPK_3388	*katY*	catalase/peroxidase HPI	YPIII_S25	**4,7**	6,7E-10
YPK_3857	*pspG*	phage shock protein G	YPIII_S25	**4,3**	1,2E-02
YPK_4131	*cpxP*	protein of unknown function Spy-related	YPIII_S25	**5,2**	1,8E-02
Information storage and processing					
Replication, cell division					
YPK_0003	*recF*	DNA replication and repair protein RecF	YPIII_E25	**8,0**	1,2E-08
YPK_0004	*gyrB*	DNA gyrase, B subunit	YPIII_E25	**5,2**	2,9E-08
YPK_0228	*dam*	DNA adenine methylase	YPIII_E25	**2,5**	9,6E-03
YPK_0465	*mreB*	cell shape determining protein, MreB/Mrl family	YPIII_E25	**5,9**	2,0E-09
YPK_0468	*maf*	maf protein	YPIII_E25	**3,0**	2,5E-02
YPK_0489	*yjgA*	ribosome-associated protein	YPIII_E25	**2,6**	5,9E-03
YPK_0659	*parE*	DNA topoisomerase IV, B subunit	YPIII_E25	**3,3**	4,4E-04
YPK_0662	*parC*	DNA topoisomerase IV, A subunit	YPIII_E25	**3,2**	6,7E-05
YPK_0820	*mutY*	A/G-specific adenine glycosylase	YPIII_E25	**4,3**	1,1E-05
YPK_0836	*ruvX*	holliday junction resolvase YqgF	YPIII_E25	**2,4**	4,6E-02
YPK_1080	*rnhB*	ribonuclease H	YPIII_E25	**5,0**	6,7E-04
YPK_1081	*dnaE*	DNA polymerase III, alpha subunit	YPIII_E25	**3,0**	2,6E-05
YPK_1179	*srmB*	DEAD/DEAH box helicase domain protein	YPIII_E25	**5,5**	5,6E-10
YPK_1693	*tatD*	hydrolase, TatD family	YPIII_E25	**3,8**	1,5E-03
YPK_2013	*nth*	endonuclease III	YPIII_E25	**2,8**	5,2E-03
YPK_2033	*topA*	DNA topoisomerase I	YPIII_E25	**2,4**	9,4E-04
YPK_2144	*ruvA*	holliday junction DNA helicase RuvA	YPIII_E25	**2,2**	1,5E-02
YPK_2145	*ruvC*	crossover junction endodeoxyribonuclease RuvC	YPIII_E25	**6,4**	4,0E-06
YPK_2147	*ntpA*	NUDIX hydrolase	YPIII_E25	**11,4**	2,8E-10
YPK_2553	*mrp*	putative ATPase Mrp	YPIII_E25	**2,0**	1,2E-02
YPK_2641	*rlmL*	putative RNA methylase	YPIII_E25	**6,1**	2,5E-09
YPK_2655	*mukB*	chromosome segregation and condensation protein MukB domain protein	YPIII_E25	**10,2**	1,5E-16
YPK_2656	*mukE*	chromosome segregation and condensation protein MukE	YPIII_E25	**6,2**	1,5E-06
YPK_2657	*mukF*	chromosome segregation and condensation protein MukF	YPIII_E25	**2,8**	7,2E-04
YPK_2667	*ihfB*	integration host factor, beta subunit	YPIII_E25	**2,2**	2,8E-03
YPK_2685	*ftsK*	cell divisionFtsK/SpoIIIE	YPIII_E25	**2,2**	4,3E-03
YPK_2846	*gyrA*	DNA gyrase, A subunit	YPIII_E25	**3,1**	8,5E-06
YPK_2898	*rhlE*	DEAD/DEAH box helicase domain protein	YPIII_E25	**38,7**	2,0E-15
YPK_3017	*holA*	DNA polymerase III, delta subunit	YPIII_E25	**6,5**	1,5E-05
YPK_3196	*recR*	recombination protein RecR	YPIII_E25	**6,2**	1,1E-09
YPK_3231	*hupB*	histone family protein DNA-binding protein	YPIII_E25	**3,7**	6,8E-06
YPK_3277	*sbcD*	nuclease SbcCD, D subunit	YPIII_E25	**8,0**	4,7E-04
YPK_3278	*sbcC*	SMC domain protein	YPIII_E25	**3,0**	3,6E-04
YPK_3280	*rdgC*	putative exonuclease RdgC	YPIII_E25	**4,2**	2,9E-06
YPK_3375	*recA*	recA protein	YPIII_E25	**2,3**	2,0E-03
YPK_3424	*mutS*	DNA mismatch repair protein MutS	YPIII_E25	**4,4**	1,1E-06
YPK_3508	*mutT*	mutator MutT protein	YPIII_E25	**2,0**	3,7E-02
YPK_3513	*ftsZ*	cell division protein FtsZ	YPIII_E25	**4,3**	2,7E-07
YPK_3514	*ftsA*	cell division protein FtsA	YPIII_E25	**2,9**	1,5E-03
YPK_3519	*ftsW*	cell division protein FtsW	YPIII_E25	**3,3**	9,6E-04
YPK_3783	*priB*	primosomal replication protein N	YPIII_E25	**80,4**	2,6E-36
YPK_3851	*uvrA*	excinuclease ABC, A subunit	YPIII_E25	**3,5**	1,6E-04
YPK_3855	*dnaB*	replicative DNA helicase	YPIII_E25	**2,2**	3,1E-02
YPK_4007	*uvrD*	DNA helicase II	YPIII_E25	**4,0**	5,7E-05
YPK_4009	*xerC*	tyrosine recombinase XerC	YPIII_E25	**4,3**	1,9E-03
YPK_4036	*rhlB*	DEAD/DEAH box helicase domain protein	YPIII_E25	**2,9**	6,0E-05
YPK_4038	*rep*	ATP-dependent DNA helicase Rep	YPIII_E25	**4,7**	2,6E-06
YPK_4102	*ftsN*	cell division protein FtsN	YPIII_E25	**3,8**	1,9E-03

Locus	Gene name	Gene description	Condition upregulated	Fold change	p-value
YPK_4152	*mutM*	formamidopyrimidine-DNA glycosylase	YPIII_E25	**4,0**	3,6E-03
YPK_4155	*radC*	DNA repair protein RadC	YPIII_E25	**2,8**	1,1E-03
YPK_4217	*gidA*	glucose inhibited division protein A	YPIII_E25	**2,4**	1,1E-03
pYV0090		putative transposase	YPIII_S25	**8,1**	1,6E-02
pYV0093		putative transposase	YPIII_S25	**14,5**	1,6E-02
YPK_0317	*smf, dprA*	DNA protecting protein DprA	YPIII_S25	**3,3**	7,5E-04
YPK_0425	*dinJ*	RelB antitoxin	YPIII_S25	**9,0**	4,7E-03
YPK_0480		putative insecticidal toxin	YPIII_S25	**6,7**	1,4E-03
YPK_0608	*fic*	filamentation induced by cAMP protein Fic	YPIII_S25	**3,8**	2,2E-02
YPK_0861	*zapA*	Z-ring-associated protein	YPIII_S25	**2,7**	4,8E-05
YPK_1055	*xni*	5'-3' exonuclease	YPIII_S25	**2,6**	2,2E-02
YPK_1142	*ccrB-1*	camphor resistance CrcB protein	YPIII_S25	**47,6**	6,5E-06
YPK_1143	*ccrB-2*	CrcB protein	YPIII_S25	**27,3**	4,8E-04
YPK_1163	*phrB*	deoxyribodipyrimidine photo-lyase	YPIII_S25	**4,7**	8,0E-05
YPK_1542	*yfcH*	cell division inhibitor	YPIII_S25	**16,8**	1,0E-14
YPK_1624	*trp14A*	transposase IS3/IS911 family protein	YPIII_S25	**4,2**	9,5E-04
YPK_1826	*ihfA*	integration host factor, alpha subunit	YPIII_S25	**3,9**	4,1E-03
YPK_1970		transposase and inactivated derivatives, TnpA family-like protein	YPIII_S25	**8,5**	5,8E-04
YPK_1984	*tus*	DNA replication terminus site-binding protein	YPIII_S25	**6,1**	5,2E-04
YPK_2122	*minD*	septum site-determining protein MinD	YPIII_S25	**2,3**	1,5E-03
YPK_2123	*minE*	cell division topological specificity factor MinE	YPIII_S25	**3,0**	1,3E-05
YPK_2292		transposase mutator type	YPIII_S25	**5,0**	4,1E-02
YPK_2307		integrase family protein	YPIII_S25	**4,2**	3,8E-03
YPK_2387	*alkA*	HhH-GPD family protein	YPIII_S25	**4,3**	4,3E-02
YPK_2439	*holE*	DNA polymerase II beta subunit	YPIII_S25	**2,6**	9,6E-03
YPK_3432	*ftsB*	septum formation initiator	YPIII_S25	**2,8**	5,8E-04
YPK_3838	*insB*	IS1 transposase	YPIII_S25	**4,2**	1,5E-02
General transcription, transcription factors, signal transduction					
YPK_0103		diguanylate phosphodiesterase	YPIII_E25	**2,5**	1,5E-02
YPK_0134	*gntR*	transcriptional regulator, LacI family	YPIII_E25	**4,0**	1,0E-02
YPK_0170	*yhgF*	RNA binding S1 domain protein	YPIII_E25	**2,1**	3,4E-02
YPK_0172	*ompR*	two component transcriptional regulator, winged helix family	YPIII_E25	**2,1**	1,9E-02
YPK_0173	*envZ*	integral membrane sensor signal transduction histidine kinase	YPIII_E25	**2,7**	3,7E-03
YPK_0308	*rpoA*	DNA-directed RNA polymerase, alpha subunit	YPIII_E25	**22,9**	3,2E-29
YPK_0334	*nusG*	NusG antitermination factor	YPIII_E25	**4,5**	2,5E-08
YPK_0340	*rpoB*	DNA-directed RNA polymerase, beta subunit	YPIII_E25	**7,5**	1,4E-14
YPK_0341	*rpoC*	DNA-directed RNA polymerase, beta' subunit	YPIII_E25	**9,7**	8,0E-18
YPK_0452	*fis*	transcriptional regulator, Fis family	YPIII_E25	**33,3**	2,1E-16
YPK_0493	*rnk*	GreA/GreB family elongation factor	YPIII_E25	**2,9**	2,6E-03
YPK_0517		BolA family protein	YPIII_E25	**2,5**	8,2E-04
YPK_0837	*algH*	putative transcriptional regulator	YPIII_E25	**5,1**	2,5E-05
YPK_1189	*rnc*	ribonuclease III	YPIII_E25	**2,8**	1,5E-03
YPK_1292	*yfgA*	transcriptional regulator, XRE family	YPIII_E25	**2,6**	3,1E-04
YPK_1327	*baeR*	two component transcriptional regulator, winged helix family	YPIII_E25	**3,9**	4,4E-02
YPK_1706	*mfd*	transcription-repair coupling factor	YPIII_E25	**3,2**	1,1E-04
YPK_1711	*cobB*	silent information regulator protein Sir2	YPIII_E25	**2,9**	1,1E-02
YPK_1781	*msrC, yebR*	GAF domain-containing protein	YPIII_E25	**2,3**	4,0E-02
YPK_1782	*proQ*	ProQ activator of osmoprotectant transporter ProP	YPIII_E25	**6,5**	7,9E-12
YPK_2016	*rnb*	exoribonuclease II	YPIII_E25	**11,9**	3,0E-16
YPK_2385		transcriptional regulator, AraC family	YPIII_E25	**4,3**	2,9E-06
YPK_2686	*lrp*	transcriptional regulator, AsnC family	YPIII_E25	**3,2**	8,6E-04
YPK_2794	*yejH*	type III restriction protein res subunit	YPIII_E25	**2,8**	4,4E-02
YPK_3256	*nusB*	NusB antitermination factor	YPIII_E25	**6,8**	9,5E-11
YPK_3337	*emrR*	transcriptional regulator, MarR family	YPIII_E25	**2,2**	1,1E-02
YPK_3378		transcriptional regulator, DeoR family	YPIII_E25	**2,2**	8,8E-03
YPK_3417		transcriptional regulator, DeoR family	YPIII_E25	**3,3**	3,7E-03
YPK_3468	*dksA*	transcriptional regulator, TraR/DksA family	YPIII_E25	**4,1**	8,4E-08
YPK_3492	*pdhR*	GntR domain protein	YPIII_E25	**7,7**	1,0E-12
YPK_3547	*rapA*	SNF2-related protein	YPIII_E25	**16,1**	1,6E-18
YPK_3731	*nusA*	NusA antitermination factor	YPIII_E25	**5,5**	1,1E-10
YPK_3739	*greA*	transcription elongation factor GreA	YPIII_E25	**7,6**	7,0E-09
YPK_3742	*basS*	integral membrane sensor signal transduction histidine kinase	YPIII_E25	**5,2**	5,1E-03
YPK_3976	*rpoH*	RNA polymerase, sigma 32 subunit, RpoH	YPIII_E25	**2,2**	1,3E-03
YPK_4027	*rffC*	TDP-D-fucosamine acetyltransferase	YPIII_E25	**2,3**	2,7E-02
YPK_4034	*rho*	transcription termination factor Rho	YPIII_E25	**4,5**	3,4E-08
YPK_4158	*slmA*	transcriptional regulator, TetR family	YPIII_E25	**7,2**	1,1E-06
YPK_4178	*spoT*	(p)ppGpp synthetase I, SpoT/RelA	YPIII_E25	**4,1**	2,5E-07
YPK_4180	*recG*	ATP-dependent DNA helicase RecG	YPIII_E25	**4,9**	9,1E-05
YPK_0060	*lacI, galR*	transcriptional regulator, AraC family	YPIII_S25	**4,0**	2,1E-02
YPK_0081	*uhpA*	two component transcriptional regulator, LuxR family	YPIII_S25	**2,5**	3,1E-02
YPK_0124		multi-sensor hybrid histidine kinase	YPIII_S25	**3,3**	4,1E-02
YPK_0131		two component transcriptional regulator, winged helix family	YPIII_S25	**3,3**	8,6E-03
YPK_0348	*rsd*	regulator of RpoD, Rsd/AlgQ	YPIII_S25	**18,9**	4,3E-23
YPK_0366	*aceK*	(Isocitrate dehydrogenase (NADP(+))) kinase	YPIII_S25	**49,7**	4,8E-11
YPK_0367	*iclR*	transcriptional regulator, IclR family	YPIII_S25	**40,4**	2,2E-27
YPK_0415		transcriptional regulator, AraC family	YPIII_S25	**4,3**	1,3E-03
YPK_0481		transcriptional regulator, LysR family	YPIII_S25		2,4E-02
YPK_0482		transcriptional regulator, LysR family	YPIII_S25	**3,9**	4,4E-02
YPK_0488	*yhcO*	barstar (barnase inhibitor)	YPIII_S25	**7,3**	1,7E-04
YPK_0505	*rpoN*	RNA polymerase, sigma 54 subunit, RpoN	YPIII_S25	**2,6**	1,8E-04
YPK_0979		transcriptional regulator, LacI family	YPIII_S25	**3,8**	2,6E-02
YPK_1086		transcriptional antiterminator, Rof	YPIII_S25	**3,9**	2,7E-06
YPK_1147	*celD*	transcriptional regulator, AraC family	YPIII_S25	**7,0**	4,2E-03
YPK_1182	*rpoE*	RNA polymerase, sigma-24 subunit, ECF subfamily	YPIII_S25	**8,2**	2,2E-15
YPK_1183	*rseA*	anti sigma-E protein, RseA	YPIII_S25	**4,5**	4,9E-08
YPK_1184	*rseB*	sigma E regulatory protein, MucB/RseB	YPIII_S25	**7,5**	1,5E-10
YPK_1185	*rseC*	positive regulator of sigma E, RseC/MucC	YPIII_S25	**5,7**	1,7E-03
YPK_1221		transcriptional regulator, XRE family	YPIII_S25	**3,2**	4,0E-03
YPK_1248		transcriptional regulator, RpiR family	YPIII_S25	**2,8**	3,7E-02
YPK_1270	*csiE*	stationary phase inducible protein CsiE	YPIII_S25	**16,8**	1,1E-11
YPK_1384	*narP*	two component transcriptional regulator, LuxR family	YPIII_S25	**2,2**	1,9E-02
YPK_1543		diguanylate phosphodiesterase	YPIII_S25	**3,7**	3,5E-02

Locus	Gene name	Gene description	Condition upregulated	Fold change	p-value
YPK_1549		transcriptional regulator, LacI family	YPIII_S25	**3,7**	7,3E-03
YPK_1615	*dmlR*	transcriptional regulator, LysR family	YPIII_S25	**21,3**	2,5E-10
YPK_1714	*phoQ*	integral membrane sensor signal transduction histidine kinase	YPIII_S25	**4,8**	5,7E-05
YPK_1715	*phoP*	two component transcriptional regulator, winged helix family	YPIII_S25	**4,7**	9,4E-06
YPK_1724	*cscR*	transcriptional regulator, LacI family	YPIII_S25	**5,7**	2,7E-02
YPK_1975		GAF modulated sigma54 specific transcriptional regulator, Fis family	YPIII_S25	**30,4**	2,9E-26
YPK_1981	*mlc*	ROK family protein	YPIII_S25	**4,3**	3,1E-05
YPK_1982	*ynfL*	transcriptional regulator, LysR family	YPIII_S25	**10,5**	6,1E-10
YPK_1988		transcriptional regulator, GntR family	YPIII_S25	**2,5**	7,5E-03
YPK_1996	*araC*	transcriptional regulator, AraC family	YPIII_S25	**20,1**	6,4E-16
YPK_2078	*rssB*	response regulator receiver protein	YPIII_S25	**18,2**	1,0E-09
YPK_2100	*prkA*	putative serine protein kinase, PrkA	YPIII_S25	**55,3**	1,7E-35
YPK_2166		putative transcriptional regulator	YPIII_S25	**2,3**	4,7E-02
YPK_2231		putative transcriptional regulator, GntR family	YPIII_S25	**2,6**	2,8E-02
YPK_2235	*phoH*	PhoH family protein	YPIII_S25	**103,0**	1,1E-46
YPK_2255		transcriptional regulator, DeoR family	YPIII_S25	**5,0**	1,4E-03
YPK_2259		transcriptional regulator, LysR family	YPIII_S25	**3,1**	1,0E-02
YPK_2269	*fimZ*	two component transcriptional regulator, LuxR family	YPIII_S25	**3,6**	7,4E-06
YPK_2310		transcriptional regulator, XRE family	YPIII_S25	**2,6**	3,4E-02
YPK_2470	*atoS1*	diguanylate cyclase with PAS/PAC sensor	YPIII_S25	**2,8**	9,6E-03
YPK_2491	*thuR*	transcriptional regulator, LacI family	YPIII_S25	**7,0**	1,2E-07
YPK_2754		transcriptional regulator, LysR family	YPIII_S25	**6,8**	3,5E-08
YPK_2899		transcriptional regulator, TetR family	YPIII_S25	**3,8**	6,5E-03
YPK_3033		transcriptional regulator, LuxR family	YPIII_S25	**21,9**	2,1E-06
YPK_3206	*acrR*	transcriptional regulator, TetR family	YPIII_S25	**5,4**	2,2E-03
YPK_3237	*bolA*	BolA family protein	YPIII_S25	**7,6**	2,8E-10
YPK_3275	*phoR*	PAS/PAC sensor signal transduction histidine kinase	YPIII_S25	**4,1**	3,7E-05
YPK_3368	*luxS*	quorum-sensing autoinducer 2 (AI-2), LuxS	YPIII_S25	**6,9**	8,0E-13
YPK_3397	*fucR*	transcriptional regulator, DeoR family	YPIII_S25	**78,4**	2,6E-11
YPK_3425	*rpoS*	RNA polymerase, sigma 70 subunit, RpoD family	YPIII_S25	**11,2**	9,9E-22
YPK_3609	*rob*	transcriptional regulator, AraC family	YPIII_S25	**3,0**	2,4E-02
YPK_3632	*osmY*	hyperosmotically inducible periplasmic protein	YPIII_S25	**15,9**	2,1E-14
YPK_3638	*hmsT*	diguanylate cyclase	YPIII_S25	**6,6**	5,6E-07
YPK_3649	*ydeW*	transcriptional regulator, DeoR family	YPIII_S25	**4,6**	4,7E-05
YPK_3661		transcriptional regulator, AraC family	YPIII_S25	**5,8**	4,1E-03
YPK_3760	*sfsB*	putative transcriptional regulator, Nlp	YPIII_S25	**38,5**	3,7E-11
YPK_3832		transcriptional regulator, TetR family	YPIII_S25	**2,6**	1,2E-02
YPK_3841	*rhaR*	transcriptional regulator, AraC family	YPIII_S25	**4,7**	6,9E-04
YPK_3896		transcriptional regulator, LysR family	YPIII_S25	**6,8**	9,9E-03
YPK_4006		transcriptional regulator, TetR family	YPIII_S25	**3,1**	6,9E-03
Translation					
YPK_0022	*glyQ*	glycyl-tRNA synthetase, alpha subunit	YPIII_E25	**5,2**	2,8E-07
YPK_0023	*glyS*	glycyl-tRNA synthetase, beta subunit	YPIII_E25	**4,6**	3,9E-08
YPK_0176	*hslR*	RNA-binding S4 domain protein	YPIII_E25	**8,3**	3,5E-07
YPK_0231	*trpS*	tryptophanyl-tRNA synthetase	YPIII_E25	**5,7**	5,1E-07
YPK_0275	*rpsL*	30S ribosomal protein S12	YPIII_E25	**11,2**	2,1E-19
YPK_0276	*rpsG*	ribosomal protein S7	YPIII_E25	**11,5**	2,6E-20
YPK_0277	*fusA*	translation elongation factor G	YPIII_E25	**13,1**	2,7E-21
YPK_0278	*tuf-1*	translation elongation factor Tu	YPIII_E25	**6,4**	6,6E-13
YPK_0282	*rpsJ*	ribosomal protein S10	YPIII_E25	**91,8**	1,3E-44
YPK_0283	*rplC*	ribosomal protein L3	YPIII_E25	**125,5**	5,2E-21
YPK_0284	*rplD*	ribosomal protein L4/L1e	YPIII_E25	**84,3**	2,5E-46
YPK_0285	*rplW*	ribosomal protein L25/L23	YPIII_E25	**88,6**	3,6E-12
YPK_0286	*rplB*	ribosomal protein L2	YPIII_E25	**76,4**	1,8E-46
YPK_0287	*rpsS*	ribosomal protein S19	YPIII_E25	**36,7**	3,4E-31
YPK_0288	*rplV*	ribosomal protein L22	YPIII_E25	**92,8**	7,6E-14
YPK_0289	*rpsC*	ribosomal protein S3	YPIII_E25	**41,2**	7,8E-29
YPK_0290	*rplP*	ribosomal protein L16	YPIII_E25	**46,2**	9,5E-16
YPK_0291	*rpmC*	ribosomal protein L29	YPIII_E25	**42,9**	3,7E-09
YPK_0292	*rpsQ*	ribosomal protein S17	YPIII_E25	**24,9**	1,3E-23
YPK_0293	*rplN*	ribosomal protein L14	YPIII_E25	**15,5**	7,2E-14
YPK_0294	*rplX*	ribosomal protein L24	YPIII_E25	**19,6**	9,2E-27
YPK_0295	*rplE*	ribosomal protein L5	YPIII_E25	**16,5**	1,5E-24
YPK_0296	*rpsN*	ribosomal protein S14	YPIII_E25	**16,5**	6,6E-25
YPK_0297	*rpsH*	ribosomal protein S8	YPIII_E25	**16,5**	8,1E-24
YPK_0298	*rplF*	ribosomal protein L6	YPIII_E25	**18,8**	4,7E-19
YPK_0299	*rplR*	ribosomal protein L18	YPIII_E25	**18,3**	1,0E-25
YPK_0300	*rpsE*	ribosomal protein S5	YPIII_E25	**24,6**	1,6E-29
YPK_0301	*rpmD*	ribosomal protein L30	YPIII_E25	**19,0**	1,0E-22
YPK_0302	*rplO*	ribosomal protein L15	YPIII_E25	**16,5**	2,3E-23
YPK_0304	*rpmJ*	ribosomal protein L36	YPIII_E25	**14,4**	8,4E-22
YPK_0305	*rpsM*	ribosomal protein S13	YPIII_E25	**17,5**	4,5E-24
YPK_0306	*rpsK*	ribosomal protein S11	YPIII_E25	**18,3**	1,3E-13
YPK_0307	*rpsD*	ribosomal protein S4	YPIII_E25	**23,2**	2,3E-29
YPK_0309	*rplQ*	ribosomal protein L17	YPIII_E25	**34,8**	5,0E-25
YPK_0314	*rsmB, sun*	16S rRNA methyltransferase B	YPIII_E25	**2,3**	5,4E-03
YPK_0332	*tuf-2*	translation elongation factor Tu	YPIII_E25	**3,2**	1,6E-05
YPK_0335	*rplK*	ribosomal protein L11	YPIII_E25	**20,0**	3,2E-27
YPK_0336	*rplA*	ribosomal protein L1	YPIII_E25	**16,1**	6,4E-25
YPK_0337	*rplJ*	ribosomal protein L10	YPIII_E25	**22,2**	1,3E-27
YPK_0338	*rplL*	ribosomal protein L7/L12	YPIII_E25	**20,2**	8,7E-08
YPK_0453	*dusB*	TIM-barrel protein, nifR3 family	YPIII_E25	**19,4**	1,4E-26
YPK_0454	*prmA*	ribosomal protein L11 methyltransferase	YPIII_E25	**4,1**	1,0E-05
YPK_0469	*cafA*	ribonuclease, Rne/Rng family	YPIII_E25	**4,2**	4,3E-04
YPK_0524	*rplM*	ribosomal protein L13	YPIII_E25	**13,9**	3,5E-22
YPK_0525	*rpsI*	ribosomal protein S9	YPIII_E25	**11,4**	4,2E-20
YPK_0636	*rpsU*	ribosomal protein S21	YPIII_E25	**11,4**	1,2E-19
YPK_0923	*prfB*	peptide chain release factor 2	YPIII_E25	**5,3**	2,7E-09
YPK_0924	*lysS*	lysyl-tRNA synthetase	YPIII_E25	**7,6**	5,3E-14
YPK_1054	*rlmM*	putative RNA 2'-O-ribose methyltransferase	YPIII_E25	**2,1**	4,5E-03
YPK_1060	*truC*	tRNA pseudouridine synthase C	YPIII_E25	**2,8**	8,1E-03
YPK_1065	*ampM*	methionine aminopeptidase, type I	YPIII_E25	**2,3**	7,2E-03
YPK_1066	*rpsB*	ribosomal protein S2	YPIII_E25	**73,2**	1,0E-44

Locus	Gene name	Gene description	Condition upregulated	Fold change	p-value
YPK_1067	*tsf*	translation elongation factor Ts	YPIII_E25	**57,6**	1,5E-40
YPK_1069	*frr*	ribosome recycling factor	YPIII_E25	**3,0**	1,5E-04
YPK_1091	*proS*	prolyl-tRNA synthetase	YPIII_E25	**8,7**	7,7E-14
YPK_1187	*lepA*	GTP-binding protein LepA	YPIII_E25	**2,4**	1,4E-03
YPK_1190	*era*	GTP-binding protein Era	YPIII_E25	**2,6**	1,1E-03
YPK_1274	*trmJ*	RNA methyltransferase, TrmH family, group 1	YPIII_E25	**2,4**	5,3E-03
YPK_1294	*hisS*	histidyl-tRNA synthetase	YPIII_E25	**2,0**	4,2E-03
YPK_1297	*engA*	small GTP-binding protein	YPIII_E25	**2,8**	1,8E-05
YPK_1437	*gltX*	glutamyl-tRNA synthetase	YPIII_E25	**2,9**	7,4E-05
YPK_1596	*rlmF*	putative SAM-dependent methyltransferase	YPIII_E25	**2,4**	1,1E-02
YPK_1677	*rne*	ribonuclease, Rne/Rng family	YPIII_E25	**2,8**	1,3E-05
YPK_1678	*rluC*	pseudouridine synthase, RluA family	YPIII_E25	**12,5**	5,5E-09
YPK_1682	*rpmF*	ribosomal protein L32	YPIII_E25	**15,3**	1,4E-17
YPK_1720	*trmU*	tRNA (5-methylaminomethyl-2-thiouridylate)-methyltransferase	YPIII_E25	**5,6**	4,4E-06
YPK_1820	*thrS*	threonyl-tRNA synthetase	YPIII_E25	**2,3**	9,3E-04
YPK_1821	*infC*	initiation factor 3	YPIII_E25	**4,1**	3,6E-07
YPK_1822	*rpmI*	ribosomal protein L35	YPIII_E25	**5,4**	3,5E-11
YPK_1823	*rplT*	ribosomal protein L20	YPIII_E25	**8,7**	5,5E-16
YPK_1824	*pheS*	phenylalanyl-tRNA synthetase, alpha subunit	YPIII_E25	**16,4**	8,4E-19
YPK_2039	*rluB*	23S rRNA pseudouridylate synthase B	YPIII_E25	**3,0**	4,7E-04
YPK_2040	*rimN*	tRNA threonylcarbamoyladenosine biosynthesis protein	YPIII_E25	**5,7**	8,9E-06
YPK_2124	*rnd*	ribonuclease D	YPIII_E25	**2,3**	1,9E-02
YPK_2148	*aspS*	aspartyl-tRNA synthetase	YPIII_E25	**10,0**	1,3E-15
YPK_2179	*prfA*	peptide chain release factor 1	YPIII_E25	**4,0**	5,7E-06
YPK_2186	*pth*	aminoacyl-tRNA hydrolase	YPIII_E25	**2,3**	8,1E-03
YPK_2187	*ychF*	GTP-binding protein YchF	YPIII_E25	**3,8**	9,6E-07
YPK_2446	*dbpA*	DEAD/DEAH box helicase domain protein	YPIII_E25	**6,9**	6,4E-08
YPK_2648	*asnC*	asparaginyl-tRNA synthetase	YPIII_E25	**5,7**	4,0E-09
YPK_2668	*rpsA*	ribosomal protein S1	YPIII_E25	**9,1**	1,4E-17
YPK_2681	*serS*	seryl-tRNA synthetase	YPIII_E25	**3,7**	1,8E-06
YPK_2691	*infA*	translation initiation factor IF-1	YPIII_E25	**14,1**	2,0E-08
YPK_2725	*rumB*	23S rRNA (uracil-5-)-methyltransferase RumB	YPIII_E25	**7,7**	7,4E-04
YPK_2777	*efp-1*	elongation factor P-like protein YeiP	YPIII_E25	**12,3**	7,3E-10
YPK_2795	*rplY*	ribosomal protein L25	YPIII_E25	**7,0**	4,1E-03
YPK_2977	*bamE, smpA*	outer membrane protein assembly factor BamE	YPIII_E25	**2,6**	1,8E-03
YPK_2994	*glnS*	glutaminyl-tRNA synthetase	YPIII_E25	**3,5**	2,5E-07
YPK_3015	*leuS*	leucyl-tRNA synthetase	YPIII_E25	**3,8**	3,1E-07
YPK_3069	*rluF*	pseudouridine synthase	YPIII_E25	**2,3**	2,0E-02
YPK_3264	*tgt*	queuine tRNA-ribosyltransferase	YPIII_E25	**3,0**	3,1E-04
YPK_3265	*queA*	S-adenosylmethionine--tRNA-ribosyltransferase-isomerase	YPIII_E25	**13,5**	2,9E-11
YPK_3318	*eif*	translation initiation factor, aIF-2BI family	YPIII_E25	**2,8**	3,9E-02
YPK_3340	*yfiF*	tRNA/rRNA methyltransferase (SpoU)	YPIII_E25	**2,5**	3,7E-03
YPK_3351	*rluD*	pseudouridine synthase, RluA family	YPIII_E25	**4,1**	2,1E-04
YPK_3361	*rplS*	ribosomal protein L19	YPIII_E25	**26,8**	3,0E-28
YPK_3362	*trmD*	tRNA (guanine-N1)-methyltransferase	YPIII_E25	**21,2**	1,5E-27
YPK_3363	*rimM*	16S rRNA processing protein RimM	YPIII_E25	**15,6**	1,7E-23
YPK_3364	*rpsP*	ribosomal protein S16	YPIII_E25	**13,8**	9,2E-21
YPK_3373	*alaS*	alanyl-tRNA synthetase	YPIII_E25	**4,7**	9,1E-09
YPK_3435	*cysN*	sulfate adenylyltransferase, large subunit	YPIII_E25	**3,9**	1,4E-02
YPK_3470	*pcnB*	poly(A) polymerase	YPIII_E25	**2,4**	8,5E-04
YPK_3588	*ileS*	isoleucyl-tRNA synthetase	YPIII_E25	**3,8**	3,6E-07
YPK_3590	*rpsT*	ribosomal protein S20	YPIII_E25	**4,9**	7,9E-10
YPK_3633	*prfC*	peptide chain release factor 3	YPIII_E25	**8,9**	7,1E-15
YPK_3636	*rsmC*	rRNA (guanine-N(2)-)-methyltransferase	YPIII_E25	**5,3**	1,0E-07
YPK_3681	*valS*	valyl-tRNA synthetase	YPIII_E25	**4,2**	1,7E-08
YPK_3724	*deaD*	DEAD/DEAH box helicase domain protein	YPIII_E25	**8,3**	6,8E-10
YPK_3726	*pnp*	polyribonucleotide nucleotidyltransferase	YPIII_E25	**5,0**	4,5E-10
YPK_3727	*rpsO*	ribosomal protein S15	YPIII_E25	**3,1**	9,8E-06
YPK_3728	*truB*	tRNA pseudouridine synthase B	YPIII_E25	**9,3**	1,4E-12
YPK_3729	*rbfA*	ribosome-binding factor A	YPIII_E25	**6,2**	1,6E-08
YPK_3730	*infB*	translation initiation factor IF-2	YPIII_E25	**9,7**	9,2E-17
YPK_3743	*obgE*	GTP-binding protein Obg/CgtA	YPIII_E25	**4,8**	9,5E-08
YPK_3756	*rpmA*	ribosomal protein L27	YPIII_E25	**16,2**	3,3E-25
YPK_3757	*rplU*	ribosomal protein L21	YPIII_E25	**17,6**	4,1E-07
YPK_3781	*rplI*	ribosomal protein L9	YPIII_E25	**45,1**	2,4E-37
YPK_3782	*rpsR*	ribosomal protein S18	YPIII_E25	**74,4**	3,8E-37
YPK_3784	*rpsF*	ribosomal protein S6	YPIII_E25	**40,7**	1,1E-25
YPK_3790	*rlmB*	23S rRNA (guanosine-2'-O-)-methyltransferase	YPIII_E25	**3,8**	1,6E-02
YPK_3797	*hflX*	GTP-binding proten HflX	YPIII_E25	**2,4**	1,8E-03
YPK_3812	*poxA*	lysyl-tRNA synthetase-related protein GenX	YPIII_E25	**4,3**	1,5E-06
YPK_3818	*efp-2*	translation elongation factor P	YPIII_E25	**9,8**	1,5E-15
YPK_3858	*dusA*	tRNA-dihydrouridine synthase A	YPIII_E25	**2,9**	3,3E-03
YPK_4074	*trmA*	tRNA (uracil-5-)-methyltransferase	YPIII_E25	**4,1**	1,1E-05
YPK_4098	*rpmE*	ribosomal protein L31	YPIII_E25	**10,6**	2,4E-17
YPK_4135	*trmL, cspR*	RNA methyltransferase, TrmH family, group 2	YPIII_E25	**20,4**	2,8E-06
YPK_4153	*rpmG*	ribosomal protein L33	YPIII_E25	**6,4**	1,5E-02
YPK_4154	*rpmB*	ribosomal protein L28	YPIII_E25	**11,4**	6,2E-19
YPK_4160	*rph*	ribonuclease PH	YPIII_E25	**5,1**	5,5E-08
YPK_4179	*trmH*	tRNA guanosine-2'-O-methyltransferase	YPIII_E25	**13,5**	1,5E-05
YPK_4188	*bipA*	GTP-binding protein TypA	YPIII_E25	**10,6**	4,7E-19
YPK_4245	*trmE*	tRNA modification GTPase TrmE	YPIII_E25	**2,8**	8,2E-04
YPK_4248	*rnpA*	ribonuclease P protein component	YPIII_E25	**15,5**	2,3E-18
YPK_4249	*rpmH*	ribosomal protein L34	YPIII_E25	**6,4**	7,6E-15
YPK_0149	*glgC*	glucose-1-phosphate adenylyltransferase	YPIII_S25	**3,6**	9,8E-04
YPK_0311	*arfA*	alternative ribosome-rescue factor	YPIII_S25	**3,3**	3,1E-04
YPK_0487		guanine-specific ribonuclease N1 and T1	YPIII_S25	**2,6**	3,2E-03
YPK_0504	*yhbH*	sigma 54 modulation protein/ribosomal protein S30EA	YPIII_S25	**9,6**	4,8E-04
YPK_1180	*trmN*	methyltransferase small	YPIII_S25	**2,1**	1,2E-02
YPK_1418		putative peptidase	YPIII_S25	**6,2**	1,4E-03
YPK_2129		endoribonuclease L-PSP	YPIII_S25	**23,4**	1,1E-08
YPK_2242		putative endopeptidase	YPIII_S25	**3,2**	8,0E-03
YPK_3353	*yfiA*	sigma 54 modulation protein/ribosomal protein S30EA	YPIII_S25	**13,3**	1,2E-23
Posttranslational modification, protein turnover					

Locus	Gene name	Gene description	Condition upregulated	Fold change	p-value
YPK_0115	*rlmJ*	23S rRNA (adenine2030-N6)-methyltransferase	YPIII_E25	**2,4**	1,4E-02
YPK_0242	*ppiA*	peptidyl-prolyl cis-trans isomerase cyclophilin type	YPIII_E25	**7,7**	4,6E-10
YPK_0268	*slyD*	peptidylprolyl isomerase FKBP-type	YPIII_E25	**8,6**	6,9E-13
YPK_0270	*fkpA*	peptidylprolyl isomerase	YPIII_E25	**2,0**	2,1E-02
YPK_0472	*tldD*	protease TldD	YPIII_E25	**5,0**	2,4E-06
YPK_0527	*sspB*	stringent starvation protein B; ClpXP protease specificity-enhancing factor	YPIII_E25	**3,4**	3,2E-05
YPK_0839	*rsmE*	16S ribosomal RNA methyltransferase RsmE	YPIII_E25	**5,7**	7,0E-06
YPK_1280	*hscA*	Fe-S protein assembly chaperone HscA	YPIII_E25	**2,6**	1,4E-03
YPK_1340	*yegD*	putative chaperone protein	YPIII_E25	**100,4**	2,3E-17
YPK_1368	*tmcA*	tRNA(Met) cytidine acetyltransferase	YPIII_E25	**2,5**	3,6E-02
YPK_1847	*sufA*	FeS assembly scaffold SufA	YPIII_E25	**4,6**	2,4E-04
YPK_1848	*sufB*	FeS assembly protein SufB	YPIII_E25	**3,5**	3,4E-06
YPK_1849	*sufC*	FeS assembly ATPase SufC	YPIII_E25	**5,5**	4,1E-08
YPK_1850	*sufD*	FeS assembly protein SufD	YPIII_E25	**7,3**	3,3E-10
YPK_1851	*sufS*	cysteine desulfurase, SufS subfamily	YPIII_E25	**4,0**	2,0E-05
YPK_1852	*sufE*	cysteine desulfuration protein SufE	YPIII_E25	**4,0**	8,9E-03
YPK_2127	*yeaZ*	peptidase M22 glycoprotease	YPIII_E25	**2,5**	1,6E-02
YPK_2620	*rlmI*	23S rRNA (cytosine1962-C5)-methyltransferase	YPIII_E25	**3,2**	9,1E-05
YPK_2633	*lonH*	Lon-like ATP-dependent protease	YPIII_E25	**6,5**	3,9E-10
YPK_2675	*ycaO*	ribosomal protein S12 methylthiotransferase	YPIII_E25	**27,4**	1,4E-20
YPK_2690	*aat*	leucyltransferase	YPIII_E25	**2,2**	1,6E-02
YPK_2851	*eco*	proteinase inhibitor I11 ecotin	YPIII_E25	**13,5**	1,5E-11
YPK_2974	*GrpE*	GrpE protein	YPIII_E25	**4,9**	2,1E-09
YPK_3020	*rlmH*	rRNA large subunit methyltransferase	YPIII_E25	**3,2**	2,6E-04
YPK_3153	*ppiB*	peptidyl-prolyl cis-trans isomerase cyclophilin type	YPIII_E25	**2,9**	3,1E-05
YPK_3230	*ppiD*	PpiC-type peptidyl-prolyl cis-trans isomerase	YPIII_E25	**5,5**	1,4E-09
YPK_3232	*lon*	ATP-dependent protease La	YPIII_E25	**8,5**	1,1E-15
YPK_3234	*clpP*	ATP-dependent Clp protease, proteolytic subunit ClpP	YPIII_E25	**2,3**	5,2E-03
YPK_3235	*tig*	trigger factor	YPIII_E25	**19,1**	5,7E-26
YPK_3427	*pcm*	protein-L-isoaspartate O-methyltransferase	YPIII_E25	**3,4**	4,1E-04
YPK_3571	*surA*	SurA domain	YPIII_E25	**4,3**	2,8E-08
YPK_3586	*fkpB*	peptidylprolyl isomerase FKBP-type	YPIII_E25	**2,4**	4,3E-03
YPK_3593	*dnaJ*	chaperone protein DnaJ	YPIII_E25	**18,0**	1,8E-21
YPK_3594	*dnaK*	chaperone protein DnaK	YPIII_E25	**13,9**	7,9E-22
YPK_3621	*radA*	DNA repair protein RadA	YPIII_E25	**2,3**	1,3E-02
YPK_3732	*rimP*	ribosome maturation factor RimP	YPIII_E25	**13,3**	7,2E-16
YPK_3736	*hflB*	ATP-dependent metalloprotease FtsH	YPIII_E25	**3,2**	7,2E-06
YPK_3778	*fklB*	peptidylprolyl isomerase FKBP-type	YPIII_E25	**5,9**	6,1E-10
YPK_3795	*hflC*	HflC protein	YPIII_E25	**5,2**	1,7E-10
YPK_3796	*hflK*	HflK protein	YPIII_E25	**5,1**	5,4E-09
YPK_3986	*tusA, sirA*	SirA family protein	YPIII_E25	**10,2**	2,1E-02
YPK_4040	*ppiC*	PpiC-type peptidyl-prolyl cis-trans isomerase	YPIII_E25	**3,8**	9,1E-03
YPK_4139	*grxC*	glutaredoxin 3	YPIII_E25	**3,4**	9,5E-05
YPK_1134	*ureE*	UreE urease accessory domain protein	YPIII_S25	**4,6**	4,9E-06
YPK_1135	*ureF*	urease accessory protein UreF	YPIII_S25	**4,5**	6,3E-03
YPK_1137	*ureD*	urease accessory protein UreD	YPIII_S25	**2,2**	2,0E-02
YPK_1504		cytochrome c-type biogenesis protein CcmI	YPIII_S25	**2,1**	5,8E-03
YPK_1784	*htpX*	HtpX domain protein	YPIII_S25	**5,1**	3,0E-09
YPK_1878	*anmK*	anhydro-N-acetylmuramic acid kinase	YPIII_S25	**9,0**	3,8E-07
YPK_1903	*tpx*	redoxin domain protein	YPIII_S25	**2,8**	2,3E-05
YPK_2679	*pflA*	pyruvate formate-lyase activating enzyme	YPIII_S25	**3,4**	2,7E-05
YPK_2692	*clpA*	ATP-dependent Clp protease, ATP-binding subunit clpA	YPIII_S25	**2,7**	4,1E-05
YPK_2980	*smpB*	SsrA-binding protein	YPIII_S25	**2,2**	8,3E-04
YPK_3452	*htrA*	protease Do	YPIII_S25	**6,5**	8,3E-12
YPK_3786	*rjfP*	peptidase S9, prolyl oligopeptidase active site domain protein	YPIII_S25	**2,6**	2,0E-02
YPK_4041		glutamine cyclotransferase	YPIII_S25	**18,4**	4,4E-02
Metabolism					
Energy production and conversion					
YPK_0114	*gor*	glutathione-disulfide reductase	YPIII_E25	**2,5**	2,0E-03
YPK_0152	*glpD*	FAD dependent oxidoreductase	YPIII_E25	**43,0**	1,3E-33
YPK_0507	*lptA*	lipopolysaccharide transport periplasmic protein LptA	YPIII_E25	**2,9**	4,4E-03
YPK_0819	*yggX*	protein-tyrosine-phosphatase	YPIII_E25	**2,4**	1,4E-02
YPK_0864	*ubiH*	2-polyprenyl-6-methoxyphenol 4-hydroxylase	YPIII_E25	**2,3**	1,0E-02
YPK_1281	*fdx*	ferredoxin, 2Fe-2S type, ISC system	YPIII_E25	**3,8**	9,1E-04
YPK_1550	*pta*	phosphate acetyltransferase	YPIII_E25	**21,8**	4,0E-25
YPK_1551	*ackA*	acetate kinase	YPIII_E25	**15,8**	1,2E-20
YPK_1561	*nuoB*	NADH-quinone oxidoreductase, B subunit	YPIII_E25	**2,4**	1,5E-03
YPK_1562	*nuoD*	NADH dehydrogenase I, D subunit	YPIII_E25	**3,6**	2,2E-07
YPK_1563	*nuoE*	NADH-quinone oxidoreductase, E subunit	YPIII_E25	**4,6**	5,6E-03
YPK_1564	*nuoF*	NADH-quinone oxidoreductase, F subunit	YPIII_E25	**3,4**	9,2E-06
YPK_1565	*nuoG*	NADH-quinone oxidoreductase, chain G	YPIII_E25	**3,7**	1,1E-06
YPK_1566	*nuoH*	NADH dehydrogenase (quinone)	YPIII_E25	**3,3**	2,0E-05
YPK_1567	*nuoI*	NADH-quinone oxidoreductase, chain I	YPIII_E25	**3,5**	1,0E-04
YPK_1568	*nuoJ*	NADH dehydrogenase (quinone)	YPIII_E25	**3,0**	2,7E-02
YPK_1569	*nuoK*	NADH-ubiquinone oxidoreductase chain 4L	YPIII_E25	**2,8**	1,8E-02
YPK_1570	*nuoL*	proton-translocating NADH-quinone oxidoreductase, chain L	YPIII_E25	**3,6**	1,8E-06
YPK_1571	*nuoM*	proton-translocating NADH-quinone oxidoreductase, chain M	YPIII_E25	**4,9**	1,3E-08
YPK_1572	*nuoN*	proton-translocating NADH-quinone oxidoreductase, chain N	YPIII_E25	**5,8**	4,8E-09
YPK_1702	*ndh*	FAD-dependent pyridine nucleotide-disulphide oxidoreductase	YPIII_E25	**4,3**	2,5E-05
YPK_1871	*nemA*	N-ethylmaleimide reductase	YPIII_E25	**4,9**	8,1E-04
YPK_2007	*rnfB*	electron transport complex, RnfABCDGE type, B subunit	YPIII_E25	**2,9**	7,2E-03
YPK_2008	*rnfC*	electron transport complex, RnfABCDGE type, C subunit	YPIII_E25	**9,2**	4,8E-11
YPK_2010	*rnfD*	electron transport complex, RnfABCDGE type, D subunit	YPIII_E25	**5,0**	8,2E-05
YPK_2072	*adhE*	iron-containing alcohol dehydrogenase	YPIII_E25	**6,0**	5,0E-12
YPK_2369	*putA*	delta-1-pyrroline-5-carboxylate dehydrogenase	YPIII_E25	**28,9**	6,9E-13
YPK_2850	*yfaE*	ferredoxin	YPIII_E25	**19,3**	2,2E-06
YPK_2966	*sucC*	succinyl-CoA synthetase, beta subunit	YPIII_E25	**2,0**	8,1E-03
YPK_2990	*fldA*	flavodoxin	YPIII_E25	**2,0**	3,0E-03
YPK_3253	*dxs*	deoxyxylulose-5-phosphate synthase	YPIII_E25	**2,2**	4,3E-03
YPK_3320	*mtnC*	2,3-diketo-5-methylthio-1-phosphopentane phosphatase	YPIII_E25	**2,6**	1,5E-02
YPK_3489	*lpdA*	dihydrolipoamide dehydrogenase	YPIII_E25	**14,3**	1,8E-21
YPK_3490	*aceF*	pyruvate dehydrogenase complex dihydrolipoamide acetyltransferase	YPIII_E25	**9,1**	5,5E-16
YPK_3536	*leuB*	3-isopropylmalate dehydrogenase	YPIII_E25	**3,3**	4,5E-02

Locus	Gene name	Gene description	Condition upregulated	Fold change	p-value
YPK_3767	*ppa*	inorganic diphosphatase	YPIII_E25	**5,6**	4,9E-11
YPK_3885	*hemN-2*	coproporphyrinogen dehydrogenase	YPIII_E25	**18,9**	2,3E-06
YPK_3935	*fre*	oxidoreductase FAD/NAD(P)-binding domain protein	YPIII_E25	**2,9**	4,4E-03
YPK_3992	*glpQ*	glycerophosphoryl diester phosphodiesterase	YPIII_E25	**5,2**	1,1E-03
YPK_4091	*ppc*	phosphoenolpyruvate carboxylase	YPIII_E25	**4,8**	3,4E-06
YPK_4113	*glpK*	glycerol kinase	YPIII_E25	**35,9**	5,2E-36
YPK_4137	*gpsA*	glycerol-3-phosphate dehydrogenase (NAD(P)(+))	YPIII_E25	**2,6**	2,8E-03
YPK_4219	*atpI*	ATP synthase I chain	YPIII_E25	**2,8**	3,5E-03
YPK_4220	*atpB*	ATP synthase F0, A subunit	YPIII_E25	**6,9**	2,6E-13
YPK_4221	*atpE*	ATP synthase F0, C subunit	YPIII_E25	**7,7**	6,6E-14
YPK_4222	*atpF*	ATP synthase F0, B subunit	YPIII_E25	**11,6**	5,2E-18
YPK_4223	*atpH*	ATP synthase F1, delta subunit	YPIII_E25	**14,7**	2,5E-22
YPK_4224	*atpA*	ATP synthase F1, alpha subunit	YPIII_E25	**15,0**	1,7E-22
YPK_4225	*atpG*	ATP synthase F1, gamma subunit	YPIII_E25	**16,7**	7,4E-22
YPK_4226	*atpD*	ATP synthase F1, beta subunit	YPIII_E25	**17,1**	3,2E-24
YPK_4227	*atpC*	ATP synthase F1, epsilon subunit	YPIII_E25	**20,2**	2,2E-05
YPK_0037	*fdoG-1*	molybdopterin oxidoreductase Fe4S4 region	YPIII_S25	**3,1**	1,2E-05
YPK_0038	*fdoG-2*	formate dehydrogenase, alpha subunit	YPIII_S25	**2,1**	2,2E-03
YPK_0174	*pckA*	phosphoenolpyruvate carboxykinase (ATP)	YPIII_S25	**7,4**	1,0E-14
YPK_0364	*aceB*	malate synthase A	YPIII_S25	**173,8**	2,3E-33
YPK_0365	*aceA*	isocitrate lyase	YPIII_S25	**114,9**	5,5E-39
YPK_0461	*yedZ*	ferric reductase domain protein transmembrane component domain	YPIII_S25	**3,4**	1,2E-02
YPK_0463	*yhdH*	quinone oxidoreductase, YhdH/YhfP family	YPIII_S25	**8,9**	1,1E-03
YPK_0486	*gabD-1*	succinic semialdehyde dehydrogenase	YPIII_S25	**5,8**	6,5E-11
YPK_0492	*cybC-1*	cytochrome b562	YPIII_S25	**12,0**	2,9E-10
YPK_0558	*sstT*	sodium:dicarboxylate symporter	YPIII_S25	**10,6**	1,4E-17
YPK_1174	*grcA*	formate C-acetyltransferase glycine radical	YPIII_S25	**2,5**	3,1E-04
YPK_1385	*napF*	ferredoxin-type protein NapF	YPIII_S25	**10,0**	2,0E-08
YPK_1387	*napA*	periplasmic nitrate reductase, large subunit	YPIII_S25	**4,3**	6,5E-07
YPK_1389	*napC*	periplasmic nitrate (or nitrite) reductase c-type cytochrome, NapC/NirT family	YPIII_S25	**7,3**	1,6E-06
YPK_1441		aldo/keto reductase	YPIII_S25	**2,4**	1,0E-02
YPK_1616	*dmlA, ttuC*	tartrate dehydrogenase	YPIII_S25	**22,2**	1,9E-04
YPK_1620	*ybbO, yohF, yeiQ, yghA*	ferredoxin	YPIII_S25	**17,2**	2,6E-05
YPK_1650		aldo/keto reductase	YPIII_S25	**10,7**	9,3E-03
YPK_1913	*nifJ*	pyruvate flavodoxin/ferredoxin oxidoreductase domain protein	YPIII_S25	**2,7**	1,4E-03
YPK_1974	*aldA*	aldehyde Dehydrogenase_	YPIII_S25	**4,9**	1,4E-03
YPK_2172		glycerophosphoryl diester phosphodiesterase	YPIII_S25	**6,9**	2,9E-02
YPK_2210		UDP-glycosyltransferase family protein	YPIII_S25	**7,3**	2,6E-03
YPK_2227	*astD*	succinylglutamic semialdehyde dehydrogenase	YPIII_S25	**22,1**	2,5E-10
YPK_2363	*wrbA*	flavoprotein WrbA	YPIII_S25	**7,2**	9,5E-10
YPK_2459	*hpaE*	5-carboxymethyl-2-hydroxymuconate semialdehyde dehydrogenase	YPIII_S25	**24,7**	6,1E-03
YPK_2506	*lldD*	FMN-dependent alpha-hydroxy acid dehydrogenase	YPIII_S25	**12,6**	8,1E-18
YPK_2614		FAD linked oxidase domain protein	YPIII_S25	**7,1**	2,0E-06
YPK_2619	*acyP*	acylphosphatase	YPIII_S25	**5,2**	1,4E-02
YPK_2622	*yccU*	CoA-binding domain protein	YPIII_S25	**6,7**	3,7E-06
YPK_2677	*pflB*	formate acetyltransferase	YPIII_S25	**3,7**	3,2E-07
YPK_2770	*xylB*	xylulokinase	YPIII_S25	**3,8**	1,4E-02
YPK_2771	*gabD-2*	aldehyde dehydrogenase	YPIII_S25	**6,9**	1,5E-07
YPK_2884	*dld*	D-lactate dehydrogenase	YPIII_S25	**32,8**	1,8E-17
YPK_2906	*morB*	NADH:flavin oxidoreductase/NADH oxidase	YPIII_S25	**3,7**	9,8E-03
YPK_3004	*ubiF*	ubiquinone biosynthesis hydroxylase, UbiH/UbiF/VisC/COQ6 family	YPIII_S25	**2,2**	1,9E-02
YPK_3049	*mmsA, iolA*	methylmalonate-semialdehyde dehydrogenase	YPIII_S25	**10,3**	5,7E-08
YPK_3343	*yfiQ*	GCN5-related N-acetyltransferase	YPIII_S25	**5,1**	3,4E-09
YPK_3403	*sgbK*	carbohydrate kinase FGGY	YPIII_S25	**6,7**	1,0E-03
YPK_3404	*fumA*	hydro-lyase, Fe-S type, tartrate/fumarate subfamily, beta subunit	YPIII_S25	**2,4**	4,1E-04
YPK_3648	*ydeV*	carbohydrate kinase FGGY	YPIII_S25	**14,0**	1,7E-08
YPK_3813	*frdA*	fumarate reductase, flavoprotein subunit	YPIII_S25	**9,3**	5,1E-13
YPK_3814	*frdB*	succinate dehydrogenase and fumarate reductase iron-sulfur protein	YPIII_S25	**12,5**	2,6E-17
YPK_3815	*frdC*	fumarate reductase subunit C	YPIII_S25	**20,6**	3,3E-15
YPK_3816	*frdD*	fumarate reductase D subunit	YPIII_S25	**25,9**	2,3E-14
YPK_3866		berberine/berberine domain protein	YPIII_S25	**4,0**	6,3E-03
Carbohydrate transport and metabolism					
YPK_0161	*glgP-2*	glycogen/starch/alpha-glucan phosphorylase	YPIII_E25	**2,3**	1,7E-02
YPK_0229	*rpe*	ribulose-phosphate 3-epimerase	YPIII_E25	**3,1**	3,8E-03
YPK_0494	*treC*	alpha,alpha-phosphotrehalase	YPIII_E25	**2,7**	4,6E-02
YPK_0850	*tktA*	transketolase	YPIII_E25	**5,8**	2,6E-11
YPK_0968	*cycB, ganO*	extracellular solute-binding protein family 1	YPIII_E25	**9,3**	5,1E-05
YPK_1273	*suhB*	inositol-phosphate phosphatase	YPIII_E25	**4,4**	1,7E-08
YPK_1401	*nanE*	N-acylglucosamine-6-phosphate 2-epimerase	YPIII_E25	**31,8**	1,7E-12
YPK_1404	*nanK*	N-acetylmannosamine kinase	YPIII_E25	**50,5**	1,4E-06
YPK_1546	*ulaA*	putative sugar-specific permease SgaT/UlaA	YPIII_E25	**8,4**	9,0E-09
YPK_1547	*ulaB*	phosphotransferase system lactose/cellobiose-specific IIB subunit	YPIII_E25	**4,0**	2,2E-03
YPK_1548	*ulaC*	putative PTS IIA-like nitrogen-regulatory protein PtsN	YPIII_E25	**13,2**	1,9E-08
YPK_1694	*ptsG*	PTS system, glucose-specific IIBC subunit	YPIII_E25	**6,5**	1,4E-09
YPK_1710	*nagK*	N-acetyl-D-glucosamine kinase	YPIII_E25	**5,0**	4,7E-03
YPK_1855	*pykF*	pyruvate kinase	YPIII_E25	**3,0**	6,4E-05
YPK_2096	*gapA*	glyceraldehyde-3-phosphate dehydrogenase, type I	YPIII_E25	**5,6**	5,7E-13
YPK_2535	*gnd*	6-phosphogluconate dehydrogenase, decarboxylating	YPIII_E25	**3,6**	1,4E-07
YPK_2728	*potH*	binding-protein-dependent transport systems inner membrane component	YPIII_E25	**4,2**	3,4E-02
YPK_3000	*nagD*	HAD-superfamily hydrolase, subfamily IIA	YPIII_E25	**2,3**	2,5E-02
YPK_3446	*eno*	phosphopyruvate hydratase	YPIII_E25	**3,6**	3,9E-07
YPK_3491	*aceE*	2-oxo-acid dehydrogenase E1 subunit, homodimeric type	YPIII_E25	**11,6**	2,3E-19
YPK_3599	*talB*	transaldolase	YPIII_E25	**2,1**	3,6E-03
YPK_3625	*deoB*	phosphopentomutase	YPIII_E25	**2,7**	2,5E-02
YPK_3887		NmrA family protein	YPIII_E25	**8,2**	3,0E-05
YPK_4081	*lpd, pdhD*	dihydrolipoamide dehydrogenase	YPIII_E25	**6,2**	1,2E-02
YPK_4112	*glpF*	MIP family channel protein	YPIII_E25	**22,2**	2,2E-24
YPK_4114	*glpX*	fructose-1,6-bisphosphatase, class II	YPIII_E25	**4,9**	1,2E-07
YPK_4141	*gpmI*	phosphoglycerate mutase, 2,3-bisphosphoglycerate-independent	YPIII_E25	**3,6**	9,8E-04
YPK_4228	*glmU*	UDP-N-acetylglucosamine pyrophosphorylase	YPIII_E25	**5,1**	4,3E-08
YPK_4229	*glmS*	glucosamine--fructose-6-phosphate aminotransferase, isomerizing	YPIII_E25	**5,2**	1,9E-08
YPK_0026	*mtlA*	PTS system, mannitol-specific IIC subunit	YPIII_S25	**4,1**	5,7E-05

Locus	Gene name	Gene description	Condition upregulated	Fold change	p-value
YPK_0057	*xylF*	D-xylose ABC transporter, periplasmic substrate-binding protein	YPIII_S25	**14,6**	3,5E-03
YPK_0111	*glxK*	glycerate kinase	YPIII_S25	**7,5**	4,4E-02
YPK_0147	*glgB*	1,4-alpha-glucan branching enzyme	YPIII_S25	**2,7**	4,5E-03
YPK_0148	*glgX*	glycogen debranching enzyme GlgX	YPIII_S25	**2,3**	2,9E-02
YPK_0150	*glgA*	glycogen/starch synthase, ADP-glucose type	YPIII_S25	**4,9**	2,5E-06
YPK_0151	*glgP-1*	glycogen/starch/alpha-glucan phosphorylase	YPIII_S25	**12,3**	6,1E-21
YPK_0413		xylose isomerase domain protein TIM barrel	YPIII_S25	**7,7**	1,2E-02
YPK_0431	*yphF-1, ytfQ-1*	carbohydrate uptake (CUT2 family) ABC transporter, periplasmic carbohydrate-binding protein	YPIII_S25	**5,9**	6,2E-08
YPK_0693	*chiC*	glycoside hydrolase family 18	YPIII_S25	**8,1**	3,7E-02
YPK_0964	*xltC*	periplasmic binding protein/LacI transcriptional regulator	YPIII_S25	**6,9**	4,2E-04
YPK_1111	*hpxB*	urate catabolism protein	YPIII_S25	**24,6**	9,7E-14
YPK_1144	*celA*	phosphotransferase system lactose/cellobiose-specific IIB subunit	YPIII_S25	**21,7**	2,9E-03
YPK_1145	*celB*	PTS system, lactose/cellobiose family IIC subunit	YPIII_S25	**3,6**	6,6E-05
YPK_1426	*crr*	PTS system, glucose subfamily, IIA subunit	YPIII_S25	**2,7**	1,0E-03
YPK_1611	*rbsB-2*	monosaccharide-transporting ATPase	YPIII_S25	**84,1**	5,5E-06
YPK_1637		glycosidase PH1107-related	YPIII_S25	**4,5**	3,3E-02
YPK_1727		NmrA family protein	YPIII_S25	**3,5**	2,4E-02
YPK_1730	*appA*	phosphoanhydride phosphorylase	YPIII_S25	**13,6**	1,1E-04
YPK_1798	*togB*	extracellular solute-binding protein family 1	YPIII_S25	**4,8**	2,0E-03
YPK_1800	*togN*	binding-protein-dependent transport systems inner membrane component	YPIII_S25		2,2E-02
YPK_1811	*yniA*	fructosamine kinase	YPIII_S25	**7,3**	9,1E-09
YPK_1963	*rbsB-3*	periplasmic binding protein/LacI transcriptional regulator	YPIII_S25	**4,0**	7,3E-04
YPK_1999	*araF*	monosaccharide-transporting ATPase	YPIII_S25	**13,7**	1,4E-06
YPK_2001	*araA*	L-arabinose isomerase	YPIII_S25	**8,9**	2,5E-03
YPK_2014		NAD-dependent epimerase/dehydratase	YPIII_S25	**31,2**	7,8E-09
YPK_2019	*mipB*	transaldolase	YPIII_S25	**2,8**	4,5E-03
YPK_2021	*araD-1*	L-ribulose-5-phosphate 4-epimerase	YPIII_S25	**9,3**	3,7E-03
YPK_2407		ribokinase-like domain-containing protein	YPIII_S25	**5,9**	1,1E-02
YPK_2410	*yphF-2, ytfQ-2*	putative sugar-binding periplasmic protein	YPIII_S25	**17,2**	3,9E-03
YPK_2411	*yphD-1, ytfT-1, yjfF-1*	monosaccharide-transporting ATPase	YPIII_S25	**16,6**	9,2E-04
YPK_2465	*manY*	PTS system, mannose/fructose/sorbose family, IIC subunit	YPIII_S25	**2,0**	1,1E-02
YPK_2466	*manZ*	PTS system, mannose/fructose/sorbose family, IID subunit	YPIII_S25	**3,6**	1,9E-07
YPK_2496		TRAP dicarboxylate transporter, DctP subunit	YPIII_S25	**8,2**	1,3E-04
YPK_2502		polysaccharide deacetylase	YPIII_S25	**103,4**	1,6E-18
YPK_2566	*mglB*	periplasmic binding protein/LacI transcriptional regulator	YPIII_S25	**3,1**	1,3E-05
YPK_2706		NAD-dependent epimerase/dehydratase	YPIII_S25	**2,3**	4,8E-02
YPK_2762	*fruA*	PTS system, fructose subfamily, IIC subunit	YPIII_S25	**8,5**	2,2E-11
YPK_2763	*fruK*	1-phosphofructokinase	YPIII_S25	**4,9**	8,4E-04
YPK_2764	*fruB*	phosphocarrier, HPr family	YPIII_S25	**4,8**	1,6E-03
YPK_2769	*rpiA*	ribose 5-phosphate isomerase	YPIII_S25	**4,4**	3,4E-02
YPK_2778	*uxuA*	mannonate dehydratase	YPIII_S25	**4,4**	2,4E-07
YPK_2823	*hyi*	hydroxypyruvate isomerase	YPIII_S25	**2,8**	2,8E-02
YPK_2825		class II aldolase/adducin family protein	YPIII_S25	**3,9**	1,7E-02
YPK_3039	*iolB*	myo-inositol catabolism IolB domain protein	YPIII_S25	**16,2**	2,3E-05
YPK_3040	*iolE*	xylose isomerase domain protein TIM barrel	YPIII_S25	**12,9**	7,5E-07
YPK_3041	*iolC*	ribokinase-like domain-containing protein	YPIII_S25	**9,9**	6,5E-09
YPK_3045	*rbsB-4*	monosaccharide-transporting ATPase	YPIII_S25	**14,4**	2,5E-13
YPK_3046	*iolG*	inositol 2-dehydrogenase	YPIII_S25	**14,5**	3,3E-08
YPK_3279	*yajF*	fructokinase	YPIII_S25	**2,0**	3,5E-02
YPK_3395	*araD-2*	L-ribulose-5-phosphate 4-epimerase	YPIII_S25	**22,1**	3,9E-04
YPK_3398	*yphF-5, ytfQ-5*	carbohydrate uptake ABC transporter 2 (CUT2) family, periplasmic carbohydrate-binding protein	YPIII_S25	**35,7**	2,5E-05
YPK_3402	*sgbU*	hexulose-6-phosphate isomerase	YPIII_S25	**4,9**	1,7E-02
YPK_3639	*ybhC*	pectinesterase	YPIII_S25	**6,1**	7,2E-06
YPK_3652	*ydeZ*	monosaccharide-transporting ATPase	YPIII_S25	**22,0**	1,1E-02
YPK_3654	*yneB*	deoxyribose-phosphate aldolase/phospho-2-dehydro-3-deoxyheptonate aldolase	YPIII_S25	**11,6**	1,7E-02
YPK_3658	*frwC*	PTS system, fructose subfamily, IIC subunit	YPIII_S25	**13,7**	8,0E-04
YPK_3659	*frwB*	PTS system, fructose-specific, IIB subunnit	YPIII_S25		1,2E-02
YPK_3707	*ycjP*	binding-protein-dependent transport systems inner membrane component	YPIII_S25	**22,3**	1,0E-09
YPK_3709	*ycjN*	extracellular solute-binding protein family 1	YPIII_S25	**52,2**	3,1E-10
YPK_3766	*fbp*	inositol phosphatase/fructose-16-bisphosphatase	YPIII_S25	**3,2**	1,7E-05
YPK_3775	*cysQ*	3'(2'),5'-bisphosphate nucleotidase	YPIII_S25	**4,1**	2,3E-05
YPK_3962	*ugpB*	extracellular solute-binding protein family 1	YPIII_S25	**9,3**	3,3E-02
YPK_4065	*yphD-2, ytfT-2, yjfF-2*	inner membrane ABC transporter permease YjfF	YPIII_S25	**2,7**	2,8E-02
YPK_4068	*yphF-6, ytfQ-6*	periplasmic binding protein/LacI transcriptional regulator	YPIII_S25	**4,2**	2,9E-05
YPK_4210	*rbsD*	RbsD or FucU transport	YPIII_S25	**14,0**	3,7E-20
Amino acid transport and metabolism					
YPK_0005	*ybhA, ybjI, yidA, yigL*	sugar phosphatase	YPIII_E25	**3,1**	2,1E-02
YPK_0014	*avtA*	aminotransferase class I and II	YPIII_E25	**5,0**	3,7E-03
YPK_0048	*mdfA*	major facilitator superfamily MFS_1	YPIII_E25	**7,1**	3,7E-06
YPK_0116	*opdA*	oligopeptidase A	YPIII_E25	**4,6**	1,3E-07
YPK_0119	*gdhA*	glutamate dehydrogenase (NADP(+))	YPIII_E25	**3,3**	4,4E-04
YPK_0225	*aroK*	shikimate kinase	YPIII_E25	**7,2**	8,0E-11
YPK_0226	*aroB*	3-dehydroquinate synthase	YPIII_E25	**3,6**	2,3E-06
YPK_0230	*gph*	phosphoglycolate phosphatase	YPIII_E25	**3,3**	1,1E-04
YPK_0238	*tsgA*	major facilitator superfamily MFS_1	YPIII_E25	**10,8**	8,2E-08
YPK_0264	*yheS*	ABC transporter related	YPIII_E25	**4,2**	5,7E-05
YPK_0380	*malK*	ABC transporter related	YPIII_E25	**14,7**	4,0E-02
YPK_0460	*aroQ*	3-dehydroquinate dehydratase, type II	YPIII_E25	**9,2**	7,3E-15
YPK_0785	*iucB*	putative siderophore biosynthesis protein IucB	YPIII_E25		3,2E-03
YPK_0788		major facilitator superfamily MFS_1	YPIII_E25	**4,2**	1,6E-02
YPK_0831	*proC*	pyrroline-5-carboxylate reductase	YPIII_E25	**3,5**	5,2E-03
YPK_0845	*speA*	arginine decarboxylase	YPIII_E25	**15,9**	3,2E-20
YPK_0867	*gcvT*	glycine cleavage system T protein	YPIII_E25	**4,5**	6,7E-05
YPK_0868	*gcsH*	glycine cleavage system H protein	YPIII_E25	**3,2**	9,8E-03
YPK_0869	*gcvP*	glycine dehydrogenase	YPIII_E25	**4,7**	4,5E-06
YPK_1022	*araJ*	major facilitator superfamily MFS_1	YPIII_E25	**7,4**	3,7E-02
YPK_1096	*metN-1*	D-methionine ABC transporter, ATPase subunit	YPIII_E25	**6,9**	1,8E-08
YPK_1167		allophanate hydrolase subunit 1	YPIII_E25	**2,9**	4,2E-03
YPK_1168		urea amidolyase related protein	YPIII_E25	**2,5**	1,8E-02
YPK_1265	*glyA*	glycine hydroxymethyltransferase	YPIII_E25	**2,9**	2,6E-04
YPK_1269	*hcaT*	chloramphenicol O-acetyltransferase	YPIII_E25	**5,8**	6,6E-06
YPK_1362	*dapA*	dihydrodipicolinate synthase	YPIII_E25	**2,2**	4,8E-03

Locus	Gene name	Gene description	Condition upregulated	Fold change	p-value
YPK_1400	*nanA*	dihydrodipicolinate synthetase	YPIII_E25	**10,6**	8,2E-13
YPK_1527	*pdxB*	D-isomer specific 2-hydroxyacid dehydrogenase NAD-binding	YPIII_E25	**3,5**	2,4E-04
YPK_1528	*asd*	aspartate-semialdehyde dehydrogenase	YPIII_E25	**3,6**	2,9E-05
YPK_1558	*alaA*	aminotransferase class I and II	YPIII_E25	**4,0**	2,9E-06
YPK_1672	*solA*	sarcosine oxidase	YPIII_E25	**2,6**	2,5E-02
YPK_1708	*lolD*	lipoprotein releasing system, ATP-binding protein	YPIII_E25	**2,3**	3,2E-02
YPK_1886	*tppB*	amino acid/peptide transporter	YPIII_E25	**6,1**	1,7E-08
YPK_1939	*arcD, lys1, lysP*	arginine/ornithine antiporter	YPIII_E25	**2,2**	2,4E-02
YPK_2041	*trpH*	PHP domain protein	YPIII_E25	**4,8**	6,9E-04
YPK_2046	*trpB*	tryptophan synthase, beta subunit	YPIII_E25	**2,3**	3,2E-02
YPK_2106	*bcr*	drug resistance transporter, Bcr/CflA subfamily	YPIII_E25	**11,4**	7,4E-06
YPK_2131	*mdtJ*	small multidrug resistance protein	YPIII_E25	**2,1**	1,9E-02
YPK_2175	*kdsA*	2-dehydro-3-deoxyphosphooctonate aldolase	YPIII_E25	**2,5**	9,9E-04
YPK_2184	*prsA*	ribose-phosphate pyrophosphokinase	YPIII_E25	**13,5**	8,1E-12
YPK_2256	*ansP*	amino acid permease-associated region	YPIII_E25	**3,6**	9,6E-04
YPK_2367	*putP*	sodium/proline symporter	YPIII_E25	**13,1**	1,4E-14
YPK_2477	*aroP*	amino acid permease-associated region	YPIII_E25	**5,3**	2,2E-08
YPK_2487	*mdlA-2*	ABC transporter related	YPIII_E25	**3,0**	2,9E-03
YPK_2517	*yeeF*	amino acid permease-associated region	YPIII_E25	**121,9**	3,3E-39
YPK_2520	*yphE-3, ytfR-3*	ABC transporter related	YPIII_E25	**4,7**	3,6E-04
YPK_2525	*hisG*	ATP phosphoribosyltransferase	YPIII_E25	**2,5**	4,4E-02
YPK_2526	*hisD*	histidinol dehydrogenase	YPIII_E25	**3,2**	1,6E-02
YPK_2581	*ybiT*	ABC transporter related	YPIII_E25	**8,5**	5,3E-13
YPK_2640	*uup*	ABC transporter related	YPIII_E25	**7,9**	1,7E-11
YPK_2670	*aroA*	3-phosphoshikimate 1-carboxyvinyltransferase	YPIII_E25	**3,1**	1,4E-03
YPK_2671	*serC*	phosphoserine aminotransferase	YPIII_E25	**2,2**	3,3E-03
YPK_2710	*artP*	ABC transporter related	YPIII_E25	**3,0**	4,7E-03
YPK_2711	*artI*	cationic amino acid ABC transporter, periplasmic binding protein	YPIII_E25	**7,5**	3,0E-05
YPK_2713	*artM*	polar amino acid ABC transporter, inner membrane subunit	YPIII_E25	**6,2**	2,9E-02
YPK_2739	*sdaC*	serine transporter	YPIII_E25	**7,7**	1,9E-13
YPK_2752	*lysP*	amino acid permease-associated region	YPIII_E25	**2,9**	2,3E-03
YPK_3158	*ybbA-1*	ABC transporter related	YPIII_E25	**6,8**	2,3E-02
YPK_3222	*mdlA-3*	ABC transporter related	YPIII_E25	**2,5**	2,6E-02
YPK_3288	*proB*	glutamate 5-kinase	YPIII_E25	**3,3**	3,5E-04
YPK_3295	*pepD*	aminoacyl-histidine dipeptidase	YPIII_E25	**3,1**	1,5E-05
YPK_3319	*mtnD, mtnZ, ADI1*	acireductone dioxygenase ARD	YPIII_E25	**3,3**	6,6E-03
YPK_3322	*ybdL*	aminotransferase class I and II	YPIII_E25	**6,5**	6,4E-04
YPK_3334		major facilitator superfamily MFS_1	YPIII_E25	**3,7**	7,4E-03
YPK_3339	*emrB*	drug resistance transporter, EmrB/QacA subfamily	YPIII_E25	**8,3**	6,2E-04
YPK_3436	*cysD*	sulfate adenylyltransferase, small subunit	YPIII_E25	**5,6**	7,9E-03
YPK_3476	*yadH*	ABC-2 type transporter	YPIII_E25	**5,4**	5,5E-05
YPK_3477	*yadG*	ABC transporter related	YPIII_E25	**7,7**	2,9E-08
YPK_3482	*speE*	spermidine synthase	YPIII_E25	**3,1**	1,3E-04
YPK_3483	*speD*	S-adenosylmethionine decarboxylase proenzyme	YPIII_E25	**2,8**	1,9E-03
YPK_3583	*carA*	carbamoyl-phosphate synthase, small subunit	YPIII_E25	**13,2**	1,5E-15
YPK_3584	*dapB*	dihydrodipicolinate reductase	YPIII_E25	**2,8**	2,5E-03
YPK_3595	*yaaH*	GPR1/FUN34/yaaH family protein	YPIII_E25	**14,5**	8,8E-12
YPK_3604	*thrA*	aspartate kinase	YPIII_E25	**3,8**	4,4E-06
YPK_3689	*ddpD-2*	ABC transporter related	YPIII_E25	**5,7**	1,1E-03
YPK_3690	*ddpF-2*	ABC transporter related	YPIII_E25	**6,1**	4,3E-02
YPK_3853	*tyrB*	aromatic-amino-acid transaminase	YPIII_E25	**2,2**	5,4E-03
YPK_3893	*hmuV*	ABC transporter related	YPIII_E25	**9,7**	3,1E-04
YPK_3978	*ftsE*	type II (general) secretory pathway (IISP) family protein	YPIII_E25	**2,4**	2,1E-02
YPK_3991	*glpA*	glycerol-3-phosphate dehydrogenase, anaerobic, A subunit	YPIII_E25	**7,7**	8,2E-04
YPK_3994	*ybhA, ybjI, yidA, yigL*	putative sugar phosphatase	YPIII_E25	**3,5**	9,2E-04
YPK_4001	*rarD*	RarD protein, DMT superfamily transporter	YPIII_E25	**3,9**	2,2E-04
YPK_4021	*mmuP, yifK*	amino acid permease-associated region	YPIII_E25	**40,7**	3,9E-13
YPK_4023	*wecF*	WzyE family protein	YPIII_E25	**3,0**	2,2E-03
YPK_4056	*ilvA*	threonine dehydratase, biosynthetic	YPIII_E25	**4,3**	9,6E-04
YPK_4057	*ilvD*	dihydroxy-acid dehydratase	YPIII_E25	**3,5**	1,9E-03
YPK_4094	*metL*	aspartate kinase	YPIII_E25	**4,1**	5,3E-05
YPK_4095	*metB*	O-succinylhomoserine (thiol)-lyase	YPIII_E25	**6,4**	9,9E-03
YPK_4144	*tdh*	L-threonine 3-dehydrogenase	YPIII_E25	**2,4**	7,1E-03
YPK_4181	*gltS*	sodium/glutamate symporter	YPIII_E25	**4,0**	1,8E-05
YPK_4189	*glnA*	glutamine synthetase, type I	YPIII_E25	**10,1**	2,1E-16
YPK_4214	*asnA*	aspartate-ammonia ligase	YPIII_E25	**7,5**	3,5E-06
pYV0007	*repB, copB*	repB, repA2, copB; putative replication transcriptional regulator	YPIII_S25	**2,1**	1,1E-02
YPK_0083	*uhpC*	phosphoglycerate transporter	YPIII_S25	**2,7**	6,1E-03
YPK_0088	*dppA*	4-phytase	YPIII_S25	**2,6**	1,8E-03
YPK_0092	*dppF*	oligopeptide/dipeptide ABC transporter, ATPase subunit	YPIII_S25	**5,1**	1,9E-05
YPK_0758	*mdlA-1*	ABC transporter related	YPIII_S25	**8,2**	1,8E-08
YPK_0762	*gntP*	gluconate transporter	YPIII_S25	**4,3**	3,0E-02
YPK_0966	*xltA*	ABC transporter related	YPIII_S25	**15,1**	6,5E-08
YPK_0978	*exuT*	major facilitator superfamily MFS_1	YPIII_S25	**7,4**	2,7E-02
YPK_1125	*ddpA-1*	extracellular solute-binding protein family 5	YPIII_S25	**18,0**	2,9E-13
YPK_1126	*ddpB-1*	binding-protein-dependent transport systems inner membrane component	YPIII_S25	**20,0**	1,4E-08
YPK_1127	*ddpC-1*	binding-protein-dependent transport systems inner membrane component	YPIII_S25	**12,5**	1,1E-03
YPK_1128	*ddpD-1*	ABC transporter related	YPIII_S25	**3,2**	1,7E-02
YPK_1129	*ddpF-1*	ABC transporter related	YPIII_S25	**6,3**	8,9E-04
YPK_1131	*ureA*	urease, gamma subunit	YPIII_S25	**5,0**	2,1E-04
YPK_1132	*ureB*	urease, beta subunit	YPIII_S25	**5,4**	3,3E-06
YPK_1133	*ureC*	urease, alpha subunit	YPIII_S25	**5,5**	1,5E-08
YPK_1136	*ureG*	urease accessory protein UreG	YPIII_S25	**3,4**	9,8E-03
YPK_1333	*ydcT*	spermidine/putrescine ABC transporter ATPase subunit	YPIII_S25	**3,5**	3,4E-02
YPK_1417	*patB, malY*	aminotransferase class I and II	YPIII_S25		1,0E-05
YPK_1538	*hisJ*	cationic amino acid ABC transporter, periplasmic binding protein	YPIII_S25	**3,4**	3,1E-05
YPK_1539	*hisQ*	polar amino acid ABC transporter, inner membrane subunit	YPIII_S25	**9,9**	5,6E-05
YPK_1541	*hisP*	ABC transporter related	YPIII_S25	**4,8**	1,4E-03
YPK_1599	*glnP*	polar amino acid ABC transporter, inner membrane subunit	YPIII_S25	**3,8**	4,4E-03
YPK_1600	*glnH*	cationic amino acid ABC transporter, periplasmic binding protein	YPIII_S25	**4,7**	3,4E-05
YPK_1610	*gutB*	alcohol dehydrogenase zinc-binding domain protein	YPIII_S25	**30,3**	4,7E-06
YPK_1612	*rbsA-2*	ABC transporter related	YPIII_S25		2,8E-03
YPK_1712	*pepT-2*	peptidase T	YPIII_S25	**4,2**	7,3E-06

Locus	Gene name	Gene description	Condition upregulated	Fold change	p-value
YPK_1837	*pmrM*	conserved hypothetical protein	YPIII_S25	**5,1**	3,5E-03
YPK_1905	*mpaA*	murein peptide amidase A	YPIII_S25	**2,2**	2,6E-02
YPK_1906	*mppA*	extracellular solute-binding protein family 5	YPIII_S25	**2,2**	3,1E-03
YPK_1928	*ydgD*	peptidase S1 and S6 chymotrypsin/Hap	YPIII_S25	**11,7**	1,2E-03
YPK_1949	*ilvN*	amino acid-binding ACT domain protein	YPIII_S25	**3,6**	3,8E-02
YPK_1950	*ilvB*	acetolactate synthase, large subunit, biosynthetic type	YPIII_S25	**3,1**	8,5E-03
YPK_1958	*tauA-2*	ABC transporter, periplasmic substrate-binding protein	YPIII_S25		1,2E-02
YPK_1983	*ynfM*	major facilitator superfamily MFS_1	YPIII_S25	**20,6**	1,8E-12
YPK_1985	*fumC*	fumarate hydratase, class II	YPIII_S25	**3,1**	5,8E-04
YPK_1997	*araH*	monosaccharide-transporting ATPase	YPIII_S25	**8,1**	1,1E-03
YPK_1998	*araG*	ABC transporter related	YPIII_S25	**22,6**	6,2E-07
YPK_2015		major facilitator superfamily MFS_1	YPIII_S25	**15,9**	5,1E-09
YPK_2030	*acnA*	aconitate hydratase 1	YPIII_S25	**32,8**	7,1E-28
YPK_2067	*oppD*	oligopeptide/dipeptide ABC transporter, ATPase subunit	YPIII_S25	**2,9**	2,6E-04
YPK_2068	*oppC*	binding-protein-dependent transport systems inner membrane component	YPIII_S25	**3,2**	9,6E-06
YPK_2069	*oppB*	alkaline phosphatase	YPIII_S25	**3,0**	1,2E-04
YPK_2070	*oppA*	extracellular solute-binding protein family 5	YPIII_S25	**4,1**	8,1E-09
YPK_2107	*dadA*	D-amino-acid dehydrogenase	YPIII_S25	**3,0**	6,6E-05
YPK_2225	*astE*	succinylglutamate desuccinylase	YPIII_S25	**22,8**	1,2E-08
YPK_2226	*astB*	succinylarginine dihydrolase	YPIII_S25	**20,0**	2,5E-10
YPK_2228	*astA*	arginine N-succinyltransferase	YPIII_S25	**27,9**	3,6E-11
YPK_2229	*astC*	succinylornithine transaminase family	YPIII_S25	**42,5**	3,6E-19
YPK_2246	*ybbA-2*	ABC transporter related	YPIII_S25	**3,2**	4,2E-03
YPK_2253		major facilitator superfamily MFS_1	YPIII_S25	**4,8**	1,2E-05
YPK_2254	*glsA*	glutaminase	YPIII_S25	**4,5**	5,6E-04
YPK_2409	*yphE-2; ytfR-2*	ABC transporter related	YPIII_S25	**7,3**	1,0E-02
YPK_2452	*hpaC*	4-hydroxyphenylacetate 3-monooxygenase, reductase subunit	YPIII_S25	**14,3**	6,6E-09
YPK_2454	*hpaX*	4-hydroxyphenylacetate transporter	YPIII_S25	**3,9**	2,2E-02
YPK_2503		major facilitator superfamily MFS_1	YPIII_S25	**133,1**	5,0E-13
YPK_2512		major facilitator superfamily MFS_1	YPIII_S25	**80,3**	2,3E-18
YPK_2565	*mglA*	ABC transporter related	YPIII_S25	**2,2**	1,7E-02
YPK_2571	*frmA, adhC*	S-(hydroxymethyl)glutathione dehydrogenase/class III alcohol dehydrogenase	YPIII_S25	**3,2**	3,9E-02
YPK_2695	*macB*	ABC transporter related	YPIII_S25	**3,0**	9,6E-04
YPK_2703	*poxB*	thiamine pyrophosphate protein TPP binding domain protein	YPIII_S25	**10,3**	8,0E-16
YPK_2705	*ltaA*	threonine aldolase	YPIII_S25	**4,9**	3,3E-06
YPK_2709	*pheA-1*	chorismate mutase	YPIII_S25	**5,8**	2,9E-09
YPK_2746		HAD-superfamily subfamily IB hydrolase, TIGR01490	YPIII_S25	**5,2**	3,5E-03
YPK_2792	*bcr*	drug resistance transporter, Bcr/CflA subfamily	YPIII_S25	**2,4**	1,0E-02
YPK_2860	*adiA*	lysine decarboxylase	YPIII_S25	**22,2**	3,8E-16
YPK_2861	*adiC*	arginine:agmatin antiporter	YPIII_S25	**144,7**	5,1E-13
YPK_2867	*ddc*	aromatic-L-amino-acid decarboxylase	YPIII_S25	**2,5**	2,2E-02
YPK_2901	*yadG, ybhF*	ABC transporter related	YPIII_S25	**3,7**	1,1E-02
YPK_2910	*xapB*	nucleoside transporter	YPIII_S25	**5,2**	3,9E-02
YPK_2932	*bioA*	adenosylmethionine-8-amino-7-oxononanoate aminotransferase	YPIII_S25	**10,5**	2,1E-06
YPK_3010	*ybeJ/gltI*	extracellular solute-binding protein family 3	YPIII_S25	**82,3**	8,5E-52
YPK_3012	*gltK*	polar amino acid ABC transporter, inner membrane subunit	YPIII_S25	**4,9**	1,4E-06
YPK_3013	*gltL*	ABC transporter related	YPIII_S25	**6,2**	9,4E-08
YPK_3043	*iatP*	monosaccharide-transporting ATPase	YPIII_S25	**7,0**	1,6E-02
YPK_3048	*iolD*	thiamine pyrophosphate protein domain protein TPP-binding	YPIII_S25	**6,5**	5,8E-03
YPK_3174	*rosA*	putative membrane efflux protein	YPIII_S25	**13,3**	9,4E-03
YPK_3225	*cof*	Cof-like hydrolase	YPIII_S25	**4,4**	1,7E-05
YPK_3494	*aroP*	amino acid permease-associated region	YPIII_S25	**5,6**	6,0E-04
YPK_3597		major facilitator superfamily MFS_1	YPIII_S25	**2,8**	1,6E-02
YPK_3650	*ego*	ABC transporter related	YPIII_S25		9,7E-04
YPK_3651	*ydeY*	monosaccharide-transporting ATPase	YPIII_S25	**48,0**	1,8E-03
YPK_3686	*ddpA-2*	extracellular solute-binding protein family 5	YPIII_S25	**3,0**	1,5E-05
YPK_3687	*ddpB-2*	binding-protein-dependent transport systems inner membrane component	YPIII_S25	**2,2**	1,2E-02
YPK_3706	*msmX, msmK, malK, sugC, ggtA, msiK*	ABC transporter related	YPIII_S25	**5,0**	2,5E-06
YPK_3840	*rhaT*	L-rhamnose-proton symporter, RhaT family, DMT superfamily	YPIII_S25	**3,7**	3,0E-02
YPK_3894	*metC*	cystathionine beta-lyase	YPIII_S25	**9,9**	8,4E-04
YPK_3923	*actP*	cation/acetate symporter ActP	YPIII_S25	**36,0**	2,6E-30
YPK_3974	*livK*	extracellular ligand-binding receptor	YPIII_S25	**8,6**	7,9E-07
Nucleotide transport and metabolism					
YPK_0356	*purD*	phosphoribosylamine--glycine ligase	YPIII_E25	**3,0**	5,3E-03
YPK_0357	*purH*	phosphoribosylaminoimidazolecarboxamide formyltransferase/IMP cyclohydrolase	YPIII_E25	**3,1**	1,5E-02
YPK_0827	*rdgB*	non-canonical purine NTP pyrophosphatase, rdgB/HAM1 family	YPIII_E25	**6,1**	2,2E-06
YPK_1036	*thyA*	thymidylate synthase	YPIII_E25	**3,7**	1,1E-05
YPK_1068	*pyrH*	uridylate kinase	YPIII_E25	**17,4**	7,8E-20
YPK_1117	*nrdE*	ribonucleoside-diphosphate reductase, alpha subunit	YPIII_E25	**11,7**	9,0E-04
YPK_1251	*tadA*	CMP/dCMP deaminase zinc-binding	YPIII_E25	**6,4**	7,7E-05
YPK_1253	*purL*	phosphoribosylformylglycinamidine synthase	YPIII_E25	**5,0**	5,5E-06
YPK_1289	*ndk*	nucleoside-diphosphate kinase	YPIII_E25	**2,7**	3,3E-05
YPK_1352	*upp*	uracil phosphoribosyltransferase	YPIII_E25	**41,4**	1,3E-10
YPK_1353	*pyrP, uraA*	uracil-xanthine permease	YPIII_E25	**2,6**	2,9E-02
YPK_1438	*nupC1*	nucleoside transporter	YPIII_E25	**17,1**	9,2E-20
YPK_1535	*purF*	amidophosphoribosyltransferase	YPIII_E25	**3,6**	3,6E-04
YPK_1675	*pyrC*	dihydroorotase, homodimeric type	YPIII_E25	**4,0**	3,4E-03
YPK_1718	*purB*	adenylosuccinate lyase	YPIII_E25	**5,9**	1,0E-07
YPK_2080	*purU*	formyltetrahydrofolate deformylase	YPIII_E25	**2,4**	3,0E-03
YPK_2132	*eda*	2-dehydro-3-deoxyphosphogluconate aldolase/4-hydroxy-2-oxoglutarate aldolase	YPIII_E25	**3,9**	3,4E-04
YPK_2552	*udk*	uridine kinase	YPIII_E25	**2,8**	9,0E-04
YPK_2561	*cdd*	cytidine deaminase	YPIII_E25	**7,3**	4,3E-07
YPK_2848	*nrdA*	ribonucleoside-diphosphate reductase, alpha subunit	YPIII_E25	**6,7**	3,2E-11
YPK_2849	*nrdB*	ribonucleoside-diphosphate reductase	YPIII_E25	**6,4**	1,2E-10
YPK_3194	*adk*	nucleoside-triphosphate--adenylate kinase	YPIII_E25	**4,8**	1,9E-08
YPK_3199	*apt*	adenine phosphoribosyltransferase	YPIII_E25	**4,6**	6,2E-07
YPK_3291	*gpt*	xanthine phosphoribosyltransferase	YPIII_E25	**10,4**	9,2E-11
YPK_3448	*mazG*	MazG family protein	YPIII_E25	**4,4**	1,1E-04
YPK_3454	*mtn*	adenosylhomocysteine nucleosidase	YPIII_E25	**3,1**	1,0E-03
YPK_3479	*hpt*	hypoxanthine phosphoribosyltransferase	YPIII_E25	**2,5**	1,3E-02
YPK_3624	*deoD*	purine nucleoside phosphorylase	YPIII_E25	**3,4**	3,0E-05
YPK_3626	*deoA*	thymidine phosphorylase	YPIII_E25	**2,4**	1,3E-03
YPK_3628	*nupC2*	nucleoside transporter	YPIII_E25	**3,2**	2,7E-03

Locus	Gene name	Gene description	Condition upregulated	Fold change	p-value
YPK_3776	*cpdB*	2',3'-cyclic-nucleotide 2'-phosphodiesterase	YPIII_E25	**3,2**	3,0E-04
YPK_3793	*purA*	adenylosuccinate synthase	YPIII_E25	**2,9**	6,2E-06
YPK_3879		conserved hypothetical protein	YPIII_E25	**5,3**	2,9E-03
YPK_3950	*udp*	uridine phosphorylase	YPIII_E25	**5,4**	3,5E-03
YPK_4157	*dut*	deoxyuridine 5'-triphosphate nucleotidohydrolase Dut	YPIII_E25	**6,6**	1,8E-07
YPK_4159	*pyrE*	orotate phosphoribosyltransferase	YPIII_E25	**5,3**	4,1E-05
YPK_4176	*gmk*	guanylate kinase	YPIII_E25	**2,4**	1,8E-03
YPK_1110	*pucI*	permease for cytosine/purines uracil thiamine allantoin	YPIII_S25	**3,8**	2,2E-02
YPK_1164		cyclic-AMP phosphodiesterase	YPIII_S25	**4,3**	4,9E-03
YPK_1993	*add*	adenosine deaminase	YPIII_S25	**2,5**	1,9E-02
YPK_2220	*hutF*	formiminoglutamate deiminase	YPIII_S25	**8,6**	3,2E-08
YPK_2911	*xapA*	xanthosine phosphorylase	YPIII_S25	**5,5**	4,3E-02
YPK_3453	*dgt*	deoxyguanosinetriphosphate triphosphohydrolase	YPIII_S25	**8,6**	2,4E-07
YPK_4015	*cyaA*	putative adenylate cyclase	YPIII_S25	**2,8**	4,6E-04
Coenzyme transport and metabolism					
YPK_0327	*birA*	bifunctional BirA, biotin operon repressor/biotin--acetyl-CoA-carboxylase ligase	YPIII_E25	**7,5**	4,5E-06
YPK_0328	*coaA*	pantothenate kinase	YPIII_E25	**5,5**	4,2E-07
YPK_0826	*hemN-1*	oxygen-independent coproporphyrinogen III oxidase	YPIII_E25	**9,1**	3,6E-07
YPK_0843	*metK*	methionine adenosyltransferase	YPIII_E25	**29,3**	4,0E-17
YPK_1048		UBA/THIF-type NAD/FAD binding protein	YPIII_E25	**5,8**	1,5E-02
YPK_2029	*ribA*	GTP cyclohydrolase II	YPIII_E25	**3,7**	2,5E-03
YPK_2568	*folE*	GTP cyclohydrolase I	YPIII_E25	**2,5**	2,2E-02
YPK_3026	*lipB*	lipoate-protein ligase B	YPIII_E25	**2,4**	1,1E-02
YPK_3027	*lipA*	lipoic acid synthetase	YPIII_E25	**3,7**	1,9E-05
YPK_3150	*folD*	methenyltetrahydrofolate cyclohydrolase	YPIII_E25	**2,4**	2,6E-03
YPK_3250	*thiI*	thiamine biosynthesis/tRNA modification protein ThiI	YPIII_E25	**22,7**	9,4E-18
YPK_3255	*thiL*	thiamine-monophosphate kinase	YPIII_E25	**4,4**	8,2E-06
YPK_3257	*ribH*	6,7-dimethyl-8-ribityllumazine synthase	YPIII_E25	**5,9**	2,7E-10
YPK_3437	*cysG*	uroporphyrin-III C-methyltransferase	YPIII_E25	**4,0**	8,7E-03
YPK_3443	*ygcM*	queuosine biosynthesis protein QueD	YPIII_E25	**10,0**	1,1E-08
YPK_3572	*pdxA*	4-hydroxythreonine-4-phosphate dehydrogenase	YPIII_E25	**3,1**	1,3E-04
YPK_3936	*ubiD*	UbiD family decarboxylase	YPIII_E25	**2,8**	2,6E-05
YPK_4105	*menA*	1,4-dihydroxy-2-naphthoate octaprenyltransferase	YPIII_E25	**3,0**	5,5E-04
YPK_4156	*dfp*	phosphopantothenoylcysteine decarboxylase/phosphopantothenate--cysteine ligase	YPIII_E25	**2,1**	2,4E-02
YPK_0860	*ygfA*	5-formyltetrahydrofolate cyclo-ligase	YPIII_S25	**2,4**	1,3E-02
YPK_1536	*ubiX*	3-octaprenyl-4-hydroxybenzoate carboxy-lyase	YPIII_S25	**3,0**	2,0E-02
YPK_1880	*pdxH*	pyridoxamine 5'-phosphate oxidase	YPIII_S25	**2,1**	2,8E-02
YPK_1980	*bioD*	dethiobiotin synthase	YPIII_S25	**9,5**	6,6E-03
YPK_2930	*bioF*	8-amino-7-oxononanoate synthase	YPIII_S25	**5,8**	8,3E-04
YPK_2931	*bioB*	biotin synthase	YPIII_S25	**13,4**	8,0E-10
YPK_3248	*panE*	2-dehydropantoate 2-reductase	YPIII_S25	**2,9**	1,3E-03
YPK_4106	*menG*	regulator of ribonuclease activity A	YPIII_S25	**2,2**	1,1E-02
YPK_4209	*rbsK*	ribokinase	YPIII_S25	**13,6**	1,8E-16
Lipid transport and metabolism					
YPK_0458	*accC*	acetyl-CoA carboxylase, biotin carboxylase	YPIII_E25	**29,5**	1,4E-26
YPK_0459	*accB*	acetyl-CoA carboxylase, biotin carboxyl carrier protein	YPIII_E25	**14,3**	2,1E-18
YPK_1077	*fabZ-1*	beta-hydroxyacyl-(acyl-carrier-protein) dehydratase FabZ	YPIII_E25	**8,7**	3,3E-11
YPK_1082	*accA*	acetyl-CoA carboxylase, carboxyl transferase, alpha subunit	YPIII_E25	**6,6**	6,1E-10
YPK_1293	*ispG*	1-hydroxy-2-methyl-2-(E)-butenyl 4-diphosphate synthase	YPIII_E25	**2,8**	9,8E-05
YPK_1683	*plsX*	fatty acid/phospholipid synthesis protein PlsX	YPIII_E25	**5,2**	3,5E-09
YPK_1684	*fabH*	3-oxoacyl-(acyl-carrier-protein) synthase III	YPIII_E25	**3,4**	5,7E-05
YPK_1685	*fabD*	malonyl CoA-acyl carrier protein transacylase	YPIII_E25	**5,5**	3,4E-04
YPK_1686	*fabG*	3-oxoacyl-(acyl-carrier-protein) reductase	YPIII_E25	**7,6**	1,3E-13
YPK_1688	*fabF*	3-oxoacyl-(acyl-carrier-protein) synthase 2	YPIII_E25	**8,9**	4,9E-14
YPK_2182	*ipk*	4-diphosphocytidyl-2C-methyl-D-erythritol kinase	YPIII_E25	**3,3**	1,3E-05
YPK_2634	*fabA*	beta-hydroxyacyl-(acyl-carrier-protein) dehydratase FabA	YPIII_E25	**2,1**	1,3E-02
YPK_2736		undecaprenyl-diphosphatase	YPIII_E25	**9,9**	2,9E-03
YPK_3430	*ispF*	2C-methyl-D-erythritol 2,4-cyclodiphosphate synthase	YPIII_E25	**2,7**	1,6E-02
YPK_3431	*ispD*	2-C-methyl-D-erythritol 4-phosphate cytidylyltransferase	YPIII_E25	**2,2**	1,1E-02
YPK_3582	*carB*	carbamoyl-phosphate synthase, large subunit	YPIII_E25	**9,3**	4,3E-14
YPK_3585	*ispH*	hydroxymethylbutenyl pyrophosphate reductase	YPIII_E25	**2,7**	7,1E-04
YPK_3810	*psd*	phosphatidylserine decarboxylase	YPIII_E25	**3,9**	1,4E-03
YPK_3862	*pslB*	glycerol-3-phosphate O-acyltransferase	YPIII_E25	**3,4**	8,0E-06
YPK_0447		3-hydroxyisobutyrate dehydrogenase	YPIII_S25	**26,0**	9,7E-04
YPK_1175	*yplA*	phospholipase A(1)	YPIII_S25		3,2E-02
YPK_1324	*yegS*	diacylglycerol kinase catalytic region	YPIII_S25	**4,3**	1,1E-02
YPK_1508	*fadI*	acetyl-CoA C-acyltransferase FadI	YPIII_S25	**2,7**	7,3E-03
YPK_1509	*fadJ*	fatty acid oxidation complex, alpha subunit FadJ	YPIII_S25	**2,7**	5,6E-04
YPK_1576	*idnO*	short-chain dehydrogenase/reductase SDR	YPIII_S25	**2,7**	3,3E-02
YPK_1976	*ydfG*	short-chain dehydrogenase/reductase SDR	YPIII_S25	**5,6**	5,7E-08
YPK_2125	*fadD-1*	AMP-dependent synthetase and ligase	YPIII_S25	**33,2**	2,9E-33
YPK_2354	*pgsA*	CDP-diacylglycerol--glycerol-3-phosphate 3-phosphatidyltransferase	YPIII_S25	**3,4**	2,4E-04
YPK_2413		short-chain dehydrogenase/reductase SDR	YPIII_S25	**5,0**	3,0E-03
YPK_2510		short-chain dehydrogenase/reductase SDR	YPIII_S25	**113,1**	2,8E-06
YPK_2606		enoyl-CoA hydratase/isomerase	YPIII_S25	**9,6**	1,2E-02
YPK_2611	*fabZ-2*	beta-hydroxyacyl-(acyl-carrier-protein) dehydratase FabA/FabZ	YPIII_S25	**36,0**	7,8E-03
YPK_2636	*fabF2*	3-oxoacyl-(acyl-carrier-protein) synthase 2	YPIII_S25	**2,2**	2,0E-02
YPK_3270		short-chain dehydrogenase/reductase SDR	YPIII_S25	**2,5**	5,0E-03
YPK_3309	*fadE*	acyl-CoA dehydrogenase	YPIII_S25	**5,9**	7,0E-09
YPK_3532	*fadD-2*	AMP-dependent synthetase and ligase	YPIII_S25	**2,3**	4,7E-02
YPK_3788	*aidB*	acyl-CoA dehydrogenase domain protein	YPIII_S25	**5,5**	1,7E-09
YPK_3933	*fadB*	fatty oxidation complex, alpha subunit FadB	YPIII_S25	**7,3**	8,5E-13
YPK_3934	*fadA*	acetyl-CoA C-acyltransferase FadA	YPIII_S25	**7,3**	1,5E-09
YPK_4151	*coaD*	pantetheine-phosphate adenylyltransferase	YPIII_S25	**2,6**	7,0E-03
Secondary metabolites biosynthesis, transport and catabolism					
YPK_0117	*rsmJ*	putative methyltransferase	YPIII_E25	**10,9**	1,4E-04
YPK_0513	*mlaE*	putative ABC transport system permease protein	YPIII_E25	**2,7**	2,6E-02
YPK_0665	*sufI*	multicopper oxidase type 3	YPIII_E25	**2,4**	3,3E-02
YPK_0783	*iucD*	L-lysine 6-monooxygenase (NADPH)	YPIII_E25	**5,9**	2,3E-04
YPK_0784	*iucC*	IucA/IucC family protein	YPIII_E25	**11,6**	7,0E-03

Locus	Gene name	Gene description	Condition upregulated	Fold change	p-value
YPK_0786	*rhbC*	IucA/IucC family protein	YPIII_E25	**49,3**	6,3E-04
YPK_0821	*trmB*	tRNA (guanine-N(7)-)-methyltransferase	YPIII_E25	**4,0**	8,7E-07
YPK_2151	*cmoA*	methyltransferase	YPIII_E25	**4,9**	7,5E-05
YPK_2152	*cmoB*	methyltransferase	YPIII_E25	**6,1**	1,7E-06
YPK_2178	*hemK, prmC*	protein-(glutamine-N5) methyltransferase, release factor-specific	YPIII_E25	**4,1**	5,7E-04
YPK_4218	*gidB*	methyltransferase GidB	YPIII_E25	**3,9**	8,3E-04
YPK_0789		intradiol ring-cleavage dioxygenase	YPIII_S25	**27,5**	2,3E-04
YPK_1846		thioesterase superfamily protein	YPIII_S25	**3,2**	9,5E-03
YPK_1858	*cfa*	cyclopropane-fatty-acyl-phospholipid synthase	YPIII_S25	**10,6**	6,4E-09
YPK_2093	*pncA*	nicotinamidase	YPIII_S25	**3,2**	6,8E-05
YPK_2453	*hpaB*	4-hydroxyphenylacetate 3-monooxygenase, oxygenase subunit	YPIII_S25	**21,1**	4,7E-05
YPK_2456	*hpaH*	2-oxo-hepta-3-ene-1,7-dioic acid hydratase	YPIII_S25	**16,9**	2,1E-02
YPK_2461	*hpaG*	4-hydroxyphenylacetate degradation bifunctional isomerase/decarboxylase, HpaG1 subunit	YPIII_S25		1,3E-03
YPK_2495		4'-phosphopantetheinyl transferase	YPIII_S25	**10,6**	1,2E-06
YPK_2509		5-oxopent-3-ene-1,2,5-tricarboxylate decarboxylase	YPIII_S25	**103,9**	7,6E-15
YPK_3921	*rcs*	acetate-CoA ligase	YPIII_S25	**61,0**	2,6E-45
YPK_3951	*ysgA*	carboxymethylenebutenolidase	YPIII_S25	**13,0**	9,9E-06
Inorganic ion transport and metabolism					
YPK_0070	*fhuB-2, fepG-2, fecD-2*	transport system permease protein	YPIII_E25	**5,5**	1,6E-03
YPK_0071	*fhuD-1, fepB-1, fecB-1*	periplasmic binding protein	YPIII_E25	**5,1**	6,1E-05
YPK_0122	*pitA*	phosphate transporter	YPIII_E25	**29,6**	1,3E-26
YPK_0782	*iutA*	TonB-dependent siderophore receptor	YPIII_E25	**76,5**	3,1E-14
YPK_0815	*fhuA, yncD*	TonB-dependent siderophore receptor	YPIII_E25	**9,8**	2,0E-11
YPK_0816	*fhuD-2, fepB-2, fecB-2*	periplasmic binding protein	YPIII_E25	**45,1**	3,6E-08
YPK_1094	*metQ-1*	lipoprotein, YaeC family	YPIII_E25	**2,3**	7,5E-03
YPK_1095	*metI*	DL-methionine transporter permease	YPIII_E25	**3,6**	6,7E-03
YPK_1341	*mgtE*	magnesium transporter	YPIII_E25	**2,2**	1,7E-02
YPK_2364	*efeB*	Dyp-type peroxidase family	YPIII_E25	**4,1**	1,2E-04
YPK_2365	*efeO*	iron uptake system component EfeO	YPIII_E25	**2,2**	1,1E-02
YPK_2366	*efeU-2*	high-affinity iron transporter	YPIII_E25	**3,4**	2,2E-03
YPK_2463	*yoaE*	integral membrane protein TerC	YPIII_E25	**2,5**	2,7E-02
YPK_2469	*fcuA*	TonB-dependent siderophore receptor	YPIII_E25	**13,1**	4,7E-16
YPK_2748	*fepA-1, cirA-1*	TonB-dependent receptor	YPIII_E25	**4,0**	2,5E-05
YPK_2749	*fhuC-2, fepC-2, fecE-2*	ABC transporter related	YPIII_E25	**3,1**	1,2E-02
YPK_2750	*fhuB-3, fepG-3, fecD-3*	transport system permease protein	YPIII_E25	**6,9**	1,8E-04
YPK_2751	*fhuD-3, fepB-3, fecB-3*	periplasmic binding protein	YPIII_E25	**7,1**	1,6E-09
YPK_2798	*yejM*	sulfatase	YPIII_E25	**2,4**	2,2E-03
YPK_3409	*fepA-2, cirA-2*	TonB-dependent receptor	YPIII_E25	**2,6**	2,7E-02
YPK_3455	*yadT*	periplasmic binding protein	YPIII_E25	**4,9**	1,5E-04
YPK_3460	*fhuB*	transport system permease protein	YPIII_E25	**8,7**	1,6E-04
YPK_3461	*fhuD*	periplasmic binding protein	YPIII_E25	**4,7**	1,8E-03
YPK_3592	*nhaA*	Na+/H+ antiporter NhaA	YPIII_E25	**2,0**	3,3E-02
YPK_3826	*dcuA*	anaerobic c4-dicarboxylate antiporter, Dcu family	YPIII_E25	**2,2**	2,2E-02
YPK_3886	*chuX*	putative heme iron utilization protein	YPIII_E25	**22,0**	4,5E-06
YPK_3888	*hemP*	hemin uptake protein	YPIII_E25	**14,8**	7,9E-04
YPK_3889	*hmuR*	TonB-dependent heme/hemoglobin receptor family protein	YPIII_E25	**18,3**	1,3E-04
YPK_3890	*hmuS*	haemin-degrading family protein	YPIII_E25	**17,6**	1,2E-04
YPK_3891	*hmuT*	periplasmic binding protein	YPIII_E25	**16,9**	1,6E-03
YPK_3892	*hmuU*	transport system permease protein	YPIII_E25	**7,9**	6,1E-04
YPK_4073	*btuB*	TonB-dependent vitamin B12 receptor	YPIII_E25	**2,6**	1,5E-03
YPK_4140		rhodanese domain protein	YPIII_E25	**5,2**	7,4E-08
YPK_4241	*yieG*	xanthine/uracil/vitamin C permease	YPIII_E25	**6,4**	6,9E-06
YPK_0013	*yidE*	YidE/YbjL duplication	YPIII_S25	**5,8**	2,9E-03
YPK_0168	*feoB*	ferrous iron transport protein B	YPIII_S25	**2,1**	1,3E-02
YPK_0169	*feoA*	FeoA family protein	YPIII_S25	**5,6**	3,0E-06
YPK_0273	*tusC*	sulfur relay protein TusC/DsrF	YPIII_S25	**3,4**	8,7E-03
YPK_0274	*tusB*	sulfur relay protein TusB/DsrH	YPIII_S25	**3,7**	1,8E-03
YPK_0778	SLC13A2_3_5	anion transporter	YPIII_S25	**11,6**	7,6E-07
YPK_1001	*cynT, can*	carbonic anhydrase	YPIII_S25	**107,3**	1,2E-12
YPK_1141	*kch*	TrkA-N domain protein	YPIII_S25	**23,0**	1,1E-16
YPK_1158	*kdpB*	K+-transporting ATPase, B subunit	YPIII_S25	**6,5**	4,6E-02
YPK_1159	*kdpA*	potassium-transporting ATPase, A subunit	YPIII_S25	**5,6**	8,4E-03
YPK_1375	*afuA, fbpA*	extracellular solute-binding protein family 1	YPIII_S25	**191,9**	9,1E-44
YPK_1376	*afuB, fbpB*	binding-protein-dependent transport systems inner membrane component	YPIII_S25	**35,0**	3,3E-20
YPK_1377	*afuC*	ABC transporter related	YPIII_S25	**26,4**	8,0E-21
YPK_1386	*napD*	NapD family protein	YPIII_S25	**4,4**	4,7E-02
YPK_1409	*cysT*	sulfate ABC transporter, inner membrane subunit	YPIII_S25	**3,9**	4,4E-02
YPK_1492	*phnA*	alkylphosphonate utilization operon protein PhnA	YPIII_S25	**3,0**	5,1E-04
YPK_1496	*ccmA*	heme exporter protein CcmA	YPIII_S25	**4,6**	1,6E-06
YPK_1607		cation diffusion facilitator family transporter	YPIII_S25	**3,4**	4,1E-03
YPK_1619		Rieske (2Fe-2S) domain protein	YPIII_S25	**26,4**	1,2E-14
YPK_1815	*yfeA*	periplasmic solute binding protein	YPIII_S25	**7,0**	4,2E-07
YPK_1907	*zntB*	Mg2 transporter protein CorA family protein	YPIII_S25	**3,0**	1,8E-04
YPK_2051		sulphate transporter	YPIII_S25	**4,2**	1,2E-03
YPK_2251		periplasmic protein p19 involved in high-affinity Fe2+ transport	YPIII_S25	**3,9**	7,2E-05
YPK_2252	*efeU-1*	iron permease FTR1	YPIII_S25	**5,0**	2,6E-07
YPK_2438	*ftnA*	ferroxidase	YPIII_S25	**3,0**	7,4E-05
YPK_2676	*focA*	formate/nitrite transporter	YPIII_S25	**2,4**	1,4E-03
YPK_2862	*opuBD-1*	binding-protein-dependent transport systems inner membrane component	YPIII_S25	**2,8**	2,5E-02
YPK_2864	*opuBD-2*	binding-protein-dependent transport systems inner membrane component	YPIII_S25	**4,8**	5,0E-03
YPK_2866	*ynjE, sseA*	rhodanese domain protein	YPIII_S25	**2,6**	9,4E-03
YPK_2877	*phnD*	phosphonate ABC transporter, periplasmic phosphonate binding protein	YPIII_S25	**20,0**	3,7E-02
YPK_2951	*zitB*	zinc transporter ZitB	YPIII_S25	**5,3**	2,1E-02
YPK_3008	*corC*	transporter-associated region	YPIII_S25	**3,0**	9,2E-05
YPK_3011	*gltJ*	polar amino acid ABC transporter, inner membrane subunit	YPIII_S25	**30,7**	4,3E-20
YPK_3165	*ATCU*	copper-translocating P-type ATPase	YPIII_S25	**5,3**	1,4E-07
YPK_3205	*ychN*	DsrE family protein	YPIII_S25	**9,9**	3,9E-06
YPK_3411	*yhjA*	cytochrome-c peroxidase	YPIII_S25	**4,5**	5,4E-03
YPK_3441	*cysI*	sulfite reductase (NADPH) hemoprotein, beta-component	YPIII_S25	**2,1**	3,8E-02
YPK_3458	*yadQ*	chloride channel core	YPIII_S25	**7,0**	1,0E-08
YPK_3614		ATPase, P-type (transporting), HAD superfamily, subfamily IC	YPIII_S25	**2,7**	2,3E-03

Locus	Gene name	Gene description	Condition upregulated	Fold change	p-value
YPK_3708	*ycjO*	binding-protein-dependent transport systems inner membrane component	YPIII_S25	**39,7**	3,6E-06
YPK_3985	*zntA*	heavy metal translocating P-type ATPase	YPIII_S25	**4,2**	7,1E-03
General membrane transport, secretion and structural proteins					
YPK_0019	*yiaD*	OmpA/MotB domain protein	YPIII_E25	**4,5**	5,8E-03
YPK_0080	*eptB*	phosphoethanolamine transferase	YPIII_E25	**6,4**	1,7E-07
YPK_0219	*mrcA*	penicillin-binding protein, 1A family	YPIII_E25	**2,8**	1,9E-04
YPK_0303	*secY*	preprotein translocase, SecY subunit	YPIII_E25	**11,7**	5,3E-21
YPK_0326	*murB*	UDP-N-acetylenolpyruvoylglucosamine reductase	YPIII_E25	**3,6**	9,0E-05
YPK_0333	*secE*	preprotein translocase, SecE subunit	YPIII_E25	**4,9**	5,6E-08
YPK_0430	*ddg*	lipid A biosynthesis lauroyl (or palmitoleoyl) acyltransferase	YPIII_E25	**25,8**	2,5E-02
YPK_0466	*mreC*	rod shape-determining protein MreC	YPIII_E25	**8,1**	6,4E-08
YPK_0467	*mreD*	rod shape-determining protein MreD	YPIII_E25	**4,6**	1,7E-03
YPK_0510	*kdsD*	D-arabinose 5-phosphate isomerase	YPIII_E25	**2,5**	1,0E-02
YPK_0672	*exbB*	tonB-system energizer ExbB	YPIII_E25	**7,3**	1,6E-11
YPK_0673	*exbD*	TonB system transport protein ExbD	YPIII_E25	**7,7**	1,1E-06
YPK_0818	*mltC*	lytic transglycosylase catalytic	YPIII_E25	**2,7**	1,2E-03
YPK_1035	*lgt*	prolipoprotein diacylglyceryl transferase	YPIII_E25	**3,2**	2,0E-04
YPK_1047	*mltA*	MltA domain protein	YPIII_E25	**2,5**	5,6E-03
YPK_1074	*yaeT*	outer membrane protein assembly complex, YaeT protein	YPIII_E25	**2,4**	2,3E-03
YPK_1075	*ompH*	outer membrane chaperone Skp (OmpH)	YPIII_E25	**2,3**	7,5E-04
YPK_1078	*lpxA*	acyl-(acyl-carrier-protein)--UDP-N-acetylglucosamine O-acyltransferase	YPIII_E25	**9,4**	5,2E-15
YPK_1079	*lpxB*	lipid-A-disaccharide synthase	YPIII_E25	**4,7**	4,6E-07
YPK_1188	*lepB*	signal peptidase I	YPIII_E25	**2,8**	1,0E-03
YPK_1363	*dapX*	NlpBDapX family lipoprotein	YPIII_E25	**3,8**	5,5E-07
YPK_1641	*mscM*	MscS Mechanosensitive ion channel	YPIII_E25	**3,4**	2,4E-02
YPK_1707	*lolC*	lipoprotein releasing system, transmembrane protein, LolC/E family	YPIII_E25	**2,4**	4,3E-03
YPK_1709	*lolE*	lipoprotein releasing system, transmembrane protein LolE	YPIII_E25	**3,8**	7,3E-04
YPK_1783	*prc*	carboxyl-terminal protease	YPIII_E25	**3,1**	3,2E-06
YPK_1831	*pmrH*	DegT/DnrJ/EryC1/StrS aminotransferase	YPIII_E25	**4,9**	7,6E-05
YPK_1832	*pmrF*	glycosyl transferase family 2	YPIII_E25	**3,5**	5,8E-03
YPK_1833	*pmrI*	NAD-dependent epimerase/dehydratase	YPIII_E25	**2,6**	2,3E-03
YPK_2055	*tonB*	TonB family protein	YPIII_E25	**3,9**	9,0E-05
YPK_2138	*msbB*	lipid A biosynthesis (KDO)2-(lauroyl)-lipid IVA acyltransferase	YPIII_E25	**4,4**	1,6E-04
YPK_2181	*lolB*	outer membrane lipoprotein LolB	YPIII_E25	**2,5**	1,9E-02
YPK_2560	*yohK*	LrgB family protein	YPIII_E25	**3,6**	4,9E-03
YPK_2630	*ompA*	OmpA domain protein transmembrane region-containing protein	YPIII_E25	**4,2**	2,7E-03
YPK_2649	*ompF*	porin Gram-negative type	YPIII_E25	**2,9**	4,2E-06
YPK_2665	*msbA*	lipid A ABC exporter, fused ATPase and inner membrane subunits MsbA	YPIII_E25	**2,5**	5,2E-04
YPK_2684	*lolA*	outer membrane lipoprotein carrier protein LolA	YPIII_E25	**2,6**	1,5E-03
YPK_2885	*pbpG*	peptidase S11 D-alanyl-D-alanine carboxypeptidase 1	YPIII_E25	**5,3**	1,4E-05
YPK_2954		tol-pal system protein YbgF	YPIII_E25	**5,1**	1,4E-09
YPK_2955	*pal*	peptidoglycan-associated lipoprotein	YPIII_E25	**5,8**	8,2E-12
YPK_2956	*tolB*	Tol-Pal system beta propeller repeat protein TolB	YPIII_E25	**3,6**	1,7E-07
YPK_3009	*lnt*	apolipoprotein N-acyltransferase	YPIII_E25	**3,7**	2,3E-03
YPK_3016	*rlpB*	rare lipoprotein B	YPIII_E25	**3,1**	2,2E-04
YPK_3021	*pbpA*	penicillin-binding protein 2	YPIII_E25	**4,2**	9,7E-06
YPK_3024	*dacA*	serine-type D-Ala-D-Ala carboxypeptidase	YPIII_E25	**6,7**	3,5E-10
YPK_3261	*secF*	protein-export membrane protein SecF	YPIII_E25	**11,7**	3,4E-15
YPK_3262	*secD*	protein-export membrane protein SecD	YPIII_E25	**14,4**	1,6E-20
YPK_3263	*yajC*	preprotein translocase, YajC subunit	YPIII_E25	**5,9**	2,6E-10
YPK_3463	*mrcB*	penicillin-binding protein 1B	YPIII_E25	**2,7**	7,1E-04
YPK_3509	*secA*	preprotein translocase, SecA subunit	YPIII_E25	**3,8**	7,4E-07
YPK_3515	*ftsQ*	polypeptide-transport-associated domain protein FtsQ-type	YPIII_E25	**3,3**	1,6E-04
YPK_3516	*ddl*	D-alanine--D-alanine ligase	YPIII_E25	**5,3**	2,5E-07
YPK_3517	*murC*	UDP-N-acetylmuramate--alanine ligase	YPIII_E25	**5,2**	8,1E-09
YPK_3518	*murG*	UDP-N-acetylglucosamine--N-acetylmuramyl-(pentapeptide) pyrophosphoryl-undecaprenol N-acetylglucosamine transferase	YPIII_E25	**4,5**	2,6E-05
YPK_3520	*murD*	UDP-N-acetylmuramoylalanine--D-glutamate ligase	YPIII_E25	**3,3**	7,9E-05
YPK_3521	*mraY*	phospho-N-acetylmuramoyl-pentapeptide-transferase	YPIII_E25	**4,4**	1,8E-06
YPK_3522	*murF*	UDP-N-acetylmuramoylalanyl-D-glutamyl-2,6-diaminopimelate--D-alanyl-D-alanyl ligase	YPIII_E25	**3,6**	3,6E-06
YPK_3523	*murE*	UDP-N-acetylmuramyl-tripeptide synthetase	YPIII_E25	**4,0**	2,1E-05
YPK_3570	*imp*	organic solvent tolerance protein	YPIII_E25	**2,2**	2,1E-03
YPK_3587	*lspA*	lipoprotein signal peptidase	YPIII_E25	**2,6**	3,1E-02
YPK_3646		O-antigen polymerase	YPIII_E25	**15,3**	3,1E-15
YPK_3647	*waaQ, rfaQ*	lipopolysaccharide heptosyltransferase III	YPIII_E25	**18,7**	1,7E-15
YPK_3733	*secG*	preprotein translocase, SecG subunit	YPIII_E25	**4,5**	1,1E-06
YPK_3811	*bspA*	MscS Mechanosensitive ion channel	YPIII_E25	**2,0**	2,6E-02
YPK_3854	*alr*	alanine racemase	YPIII_E25	**2,5**	1,9E-02
YPK_3999	*pldA*	phospholipase A(2)	YPIII_E25	**2,7**	9,7E-03
YPK_4022	*wecG*	glycosyl transferase, WecB/TagA/CpsF family	YPIII_E25	**2,2**	2,6E-02
YPK_4024	*wecF, rffT*	4-alpha-L-fucosyltransferase	YPIII_E25	**7,7**	5,9E-06
YPK_4026	*rffA*	TDP-4-keto-6-deoxy-D-glucose transaminase	YPIII_E25	**2,8**	2,8E-02
YPK_4030	*wecC*	nucleotide sugar dehydrogenase	YPIII_E25	**3,0**	6,9E-04
YPK_4032	*wzzE*	lipopolysaccharide biosynthesis protein	YPIII_E25	**2,1**	2,0E-02
YPK_4138	*secB*	protein-export protein SecB	YPIII_E25	**2,6**	1,1E-03
YPK_4146	*rfaD*	ADP-L-glycero-D-manno-heptose-6-epimerase	YPIII_E25	**2,0**	2,8E-03
YPK_4147	*rfaF*	lipopolysaccharide heptosyltransferase II	YPIII_E25	**4,6**	1,5E-07
YPK_4148	*rfaC*	lipopolysaccharide heptosyltransferase I	YPIII_E25	**3,0**	1,4E-03
YPK_4194	*engB*	ribosome biogenesis GTP-binding protein YsxC	YPIII_E25	**2,0**	3,6E-02
YPK_4246	*yidC*	60 kDa inner membrane insertion protein	YPIII_E25	**25,0**	6,3E-27
YPK_0104	*yhjG*	AsmA family protein	YPIII_S25	**8,8**	8,9E-09
YPK_0473	*tccC*	insecticidal toxin complex protein TccC	YPIII_S25	**3,7**	4,3E-02
YPK_0583	*yapF*	outer membrane autotransporter barrel domain protein	YPIII_S25	**3,7**	6,3E-05
YPK_0743	*yapH*	outer membrane autotransporter barrel domain protein	YPIII_S25	**5,4**	1,3E-07
YPK_0806		peptidase M23B	YPIII_S25	**4,5**	3,6E-02
YPK_1105	*mltD*	lytic transglycosylase catalytic	YPIII_S25	**4,1**	1,1E-07
YPK_1423	*macA-1*	efflux transporter, RND family, MFP subunit	YPIII_S25	**6,8**	3,1E-02
YPK_1604		GCN5-related N-acetyltransferase	YPIII_S25	**4,7**	2,2E-03
YPK_1618	*yeaV*	putative betaine/carnitine transporter	YPIII_S25	**12,5**	2,4E-04
YPK_1621		polypeptide-transport-associated domain protein ShlB-type	YPIII_S25	**10,1**	6,5E-03
YPK_1665	*htrB*	lipid A biosynthesis lauroyl (or palmitoleoyl) acyltransferase	YPIII_S25	**8,2**	7,3E-09
YPK_1792	*ogl*	oligogalacturonide lyase	YPIII_S25	**3,8**	6,2E-07
YPK_1816	*mltE*	lytic transglycosylase catalytic	YPIII_S25	**2,4**	7,9E-03

Locus	Gene name	Gene description	Condition upregulated	Fold change	p-value
YPK_1817	*marC*	multiple antibiotic resistance (MarC)-related protein	YPIII_S25	**3,8**	8,5E-03
YPK_1838	*nlpC*	NLP/P60 protein	YPIII_S25	**3,5**	1,2E-03
YPK_1904		mandelate racemase/muconate lactonizing protein	YPIII_S25	**3,7**	1,7E-02
YPK_2002	*rtxE*	type I secretion system ATPase	YPIII_S25	**5,0**	6,3E-05
YPK_2004	*rtxB*	type I secretion system ATPase	YPIII_S25	**6,7**	1,7E-03
YPK_2022	*osmB*	osmotically inducible lipoprotein B precursor	YPIII_S25	**8,6**	2,9E-10
YPK_2126	*slp, yeaY*	outer membrane lipoprotein, Slp family	YPIII_S25	**7,2**	1,6E-11
YPK_2224	*ompC-1*	porin Gram-negative type	YPIII_S25	**4,9**	4,9E-04
YPK_2508		mandelate racemase/muconate lactonizing protein	YPIII_S25	**33,1**	4,8E-20
YPK_2678		glycosyl transferase family 25	YPIII_S25	**2,9**	2,4E-03
YPK_2696	*macA-2*	efflux transporter, RND family, MFP subunit	YPIII_S25	**2,6**	3,5E-02
YPK_2857	*ompC-3*	porin Gram-negative type	YPIII_S25	**4,6**	5,0E-02
YPK_2865	*opuC*	substrate-binding region of ABC-type glycine betaine transport system	YPIII_S25	**5,1**	2,2E-06
YPK_2914	*betT*	choline/carnitine/betaine transporter	YPIII_S25	**2,7**	1,4E-02
YPK_3064	*yapC*	outer membrane autotransporter barrel domain protein	YPIII_S25	**3,4**	1,7E-03
YPK_3204	*kefA*	MscS Mechanosensitive ion channel	YPIII_S25	**5,0**	7,3E-08
YPK_3312	*rscA*	filamentous haemagglutinin family outer membrane protein	YPIII_S25	**2,3**	2,9E-02
YPK_3426	*nlpD*	peptidase M23B	YPIII_S25	**5,6**	3,2E-12
YPK_3643		efflux transporter, RND family, MFP subunit	YPIII_S25	**2,5**	2,0E-03
YPK_3717	*ibeB*	RND efflux system, outer membrane lipoprotein, NodT family	YPIII_S25	**2,4**	1,5E-02
YPK_3865		outer membrane autotransporter barrel domain protein	YPIII_S25	**5,8**	1,8E-03
YPK_3942	*tatA*	twin-arginine translocation protein, TatA/E family subunit	YPIII_S25	**2,1**	1,9E-03
Defense mechanisms					
YPK_0640	*uppP*	undecaprenol kinase	YPIII_E25	**10,5**	8,2E-07
YPK_0739		transporter, hydrophobe/amphiphile efflux-1 (HAE1) family	YPIII_E25	**5,0**	1,6E-02
YPK_2836	*ampH*	beta-lactamase	YPIII_E25	**2,6**	1,4E-02
YPK_3338	*emrA*	efflux pump membrane protein	YPIII_E25	**13,4**	3,9E-05
YPK_3672	*hsdM-2*	type I restriction-modification system, M subunit	YPIII_E25	**6,2**	2,6E-09
YPK_4025	*wzxE*	polysaccharide biosynthesis protein	YPIII_E25	**2,2**	4,0E-02
YPK_0596	*mdtN*	multidrug resistance protein MdtN	YPIII_S25	**4,5**	4,8E-03
YPK_1422	*macB*	ABC transporter related	YPIII_S25	**4,3**	4,8E-02
YPK_1644	*cas-1*	CRISPR-associated protein Cas1	YPIII_S25	**7,9**	3,5E-04
YPK_1645	*cas-3*	CRISPR-associated helicase Cas3 family	YPIII_S25	**5,2**	1,7E-03
YPK_1648	*csy-3*	CRISPR-associated protein, Csy3 family	YPIII_S25	**3,5**	1,6E-03
YPK_1676		antibiotic biosynthesis monooxygenase	YPIII_S25	**3,1**	5,7E-03
YPK_1760	*cwlA, xlyA, xlyB*	N-acetylmuramyl-L-alanine amidase, negative regulator of AmpC, AmpD	YPIII_S25	**4,0**	5,6E-04
YPK_1794	*ybjR*	N-acetylmuramyl-L-alanine amidase, negative regulator of AmpC, AmpD	YPIII_S25	**3,0**	4,3E-03
YPK_1856	*mdtK, dinF*	MATE efflux family protein	YPIII_S25	**3,5**	3,5E-03
YPK_2247	*ybbP-1*	putative ABC transport system permease protein	YPIII_S25	**3,8**	1,1E-02
YPK_2248	*ybbP-2*	putative ABC transport system permease protein	YPIII_S25	**2,6**	2,3E-02
YPK_3044	*rbsA-4*	ABC transporter related	YPIII_S25	**15,9**	5,3E-12
YPK_3496	*ampD*	N-acetylmuramyl-L-alanine amidase, negative regulator of AmpC, AmpD	YPIII_S25	**4,7**	8,2E-05
YPK_3642	*mexB*	acriflavin resistance protein	YPIII_S25	**2,7**	1,6E-04
YPK_3655	*yneC*	antibiotic biosynthesis monooxygenase	YPIII_S25	**19,4**	8,8E-03
Others, phage-associated					
YPK_0123	*yhiN*	HI0933 family protein	YPIII_E25	**2,2**	8,4E-03
YPK_0158	*glpG*	Rhomboid family protein	YPIII_E25	**2,1**	1,5E-02
YPK_0177	*yrfG-1, yigB-1, yihX-1*	HAD-superfamily hydrolase, subfamily IA, variant 3	YPIII_E25	**2,2**	2,6E-02
YPK_0178		Intracellular growth attenuator IgaA	YPIII_E25	**3,7**	2,2E-04
YPK_0643		adenylate cyclase	YPIII_E25	**2,5**	5,8E-04
YPK_0661	*mdaB*	putative modulator of drug activity	YPIII_E25	**3,8**	4,4E-03
YPK_0862	*ygfB*	yecA family protein	YPIII_E25	**3,0**	8,1E-04
YPK_0986		glycosyl hydrolase family 88	YPIII_E25	**8,2**	3,4E-02
YPK_1169	*ybgL*	LamB/YcsF family protein	YPIII_E25	**3,5**	1,8E-03
YPK_1282		FeS assembly protein IscX	YPIII_E25	**8,0**	7,8E-06
YPK_1296	*yfgL*	outer membrane assembly lipoprotein YfgL	YPIII_E25	**2,1**	5,0E-03
YPK_1518		YfcL protein	YPIII_E25	**2,6**	2,6E-02
YPK_1534	*cvpA*	colicin V production protein	YPIII_E25	**4,4**	2,4E-02
YPK_1557	*yfbR*	metal dependent phosphohydrolase	YPIII_E25	**3,0**	2,9E-03
YPK_1719	*hflD*	high frequency lysogenization protein	YPIII_E25	**4,8**	8,3E-05
YPK_1808		2-deoxyglucose-6-phosphatase	YPIII_E25	**2,2**	2,6E-02
YPK_1853	*erfK*	ErfK/YbiS/YcfS/YnhG family protein	YPIII_E25	**3,4**	8,3E-06
YPK_1952		putative virulence factor	YPIII_E25	**7,5**	3,6E-05
YPK_2176		putative transcriptional regulator	YPIII_E25	**2,8**	1,6E-03
YPK_2362		Kelch repeat-containing protein	YPIII_E25	**2,5**	3,0E-02
YPK_2638	*pqiB*	mammalian cell entry related domain protein	YPIII_E25	**2,2**	5,8E-03
YPK_2639	*pqiA*	integral membrane protein, PqiA family	YPIII_E25	**2,0**	4,8E-02
YPK_2796	*ndpA*	nucleoid-associated protein NdpA	YPIII_E25	**2,5**	1,1E-03
YPK_2989		CopG domain protein DNA-binding domain protein	YPIII_E25	**3,9**	8,8E-04
YPK_3151	*ybcJ*	ribosome-associated protein	YPIII_E25	**2,1**	4,2E-02
YPK_3676		integrase family protein	YPIII_E25	**2,5**	1,2E-02
YPK_3987	*yhhQ*	conserved hypothetical integral membrane protein	YPIII_E25	**2,7**	3,3E-02
YPK_4008	*yrfG-3, yigB-3, yihX-3*	flavin mononucleotide phosphatase	YPIII_E25	**2,8**	7,8E-03
YPK_4244	*fabV*	trans-2-enoyl-CoA reductase	YPIII_E25	**3,9**	7,9E-07
YPK_0187		phage baseplate assembly protein V	YPIII_S25	**5,4**	5,8E-06
YPK_0269	*slyX*	SlyX family protein	YPIII_S25	**5,3**	5,0E-09
YPK_0414		oxidoreductase domain protein	YPIII_S25	**3,9**	5,5E-03
YPK_0446		beta-lactamase domain protein	YPIII_S25	**8,1**	1,7E-02
YPK_0534	*elbB*	ThiJ/PfpI domain protein	YPIII_S25	**3,4**	1,7E-04
YPK_0544	*yphA, yqjF*	putative oxidoreductase	YPIII_S25	**7,9**	4,8E-04
YPK_0570	*terY*	von Willebrand factor type A	YPIII_S25	**7,2**	1,5E-04
YPK_0667	*dkgA-1*	2,5-didehydrogluconate reductase	YPIII_S25	**3,8**	2,9E-04
YPK_0692	*cpbD-1*	fibronectin type III domain protein	YPIII_S25	**2,5**	1,8E-02
YPK_0794		lipoprotein	YPIII_S25	**7,5**	3,5E-03
YPK_0895		transcriptional activator Ogr/delta	YPIII_S25	**4,4**	2,5E-02
YPK_0944		putative portal vertex protein	YPIII_S25	**7,6**	3,1E-02
YPK_1148	*chbG*	YdjC family protein	YPIII_S25	**8,6**	2,8E-02
YPK_1416	*yfbK*	von Willebrand factor type A	YPIII_S25	**6,5**	2,8E-11
YPK_1494	*lemA*	LemA family protein	YPIII_S25	**4,6**	4,6E-02
YPK_1586		protein RhiA	YPIII_S25	**35,4**	1,1E-06
YPK_1768		patatin	YPIII_S25	**2,5**	1,3E-02

Locus	Gene name	Gene description	Condition upregulated	Fold change	p-value
YPK_1773		spore coat U domain protein	YPIII_S25	**9,3**	4,3E-03
YPK_1797		oligogalacturonate-specific porin	YPIII_S25	**4,4**	2,4E-02
YPK_1870	*sepC*	Rhs family protein-like protein	YPIII_S25	**177,8**	8,8E-25
YPK_1916		putative lipoprotein	YPIII_S25	**5,6**	5,4E-03
YPK_1931		YceI family protein	YPIII_S25	**4,9**	1,3E-02
YPK_1994	*yfeH*	putative sodium/bile acid symporter family protein	YPIII_S25	**2,3**	3,0E-02
YPK_1995		oxidoreductase domain protein	YPIII_S25	**2,7**	8,5E-04
YPK_2048		transport-associated	YPIII_S25	**27,9**	4,5E-23
YPK_2108	*spoVR*	SpoVR family protein	YPIII_S25	**31,4**	3,0E-28
YPK_2241	*hmsH*	tetratricopeptide TPR_2 repeat protein	YPIII_S25	**2,4**	4,8E-02
YPK_2249		YHS domain protein	YPIII_S25	**3,4**	3,5E-02
YPK_2260		amidohydrolase 2	YPIII_S25	**9,5**	3,0E-05
YPK_2305		late control D family protein	YPIII_S25	**5,4**	2,1E-02
YPK_2326		putative W protein (Enterobacteria phage 186)	YPIII_S25	**7,0**	2,6E-03
YPK_2388	*doc*	death-on-curing family protein	YPIII_S25	**3,0**	6,8E-04
YPK_2489		YCII-related	YPIII_S25	**3,0**	2,1E-03
YPK_2666	*comEC*	DNA internalization-related competence protein ComEC/Rec2	YPIII_S25	**2,1**	4,6E-02
YPK_2809		putative bacteriophage tail fiber protein	YPIII_S25	**6,7**	3,1E-02
YPK_2811		baseplate J family protein	YPIII_S25	**34,0**	2,7E-02
YPK_2819		Mu tail sheath family protein	YPIII_S25	**7,1**	4,8E-03
YPK_2834		beta-lactamase domain protein	YPIII_S25	**3,3**	2,9E-02
YPK_2947	*psiF*	PsiF repeat protein	YPIII_S25	**7,2**	4,1E-06
YPK_3042		oxidoreductase domain protein	YPIII_S25	**8,1**	9,3E-04
YPK_3075	*dkgA-2*	2,5-didehydrogluconate reductase	YPIII_S25	**13,5**	3,1E-11
YPK_3076		aldo/keto reductase	YPIII_S25	**12,6**	1,5E-12
YPK_3091		tail assembly chaperone gp38	YPIII_S25	**6,4**	1,2E-06
YPK_3186		LPS side chain defect: putative O-antigen transferase	YPIII_S25	**2,5**	1,7E-02
YPK_3228	*ybaW*	thioesterase superfamily protein	YPIII_S25	**18,0**	1,1E-14
YPK_3293	*cpbD-2*	chitin-binding domain 3 protein	YPIII_S25	**9,3**	1,4E-03
YPK_3359	*dcuB*	anaerobic c4-dicarboxylate antiporter, Dcu family	YPIII_S25	**5,3**	8,5E-03
YPK_3438		YcfA family protein	YPIII_S25	**5,0**	2,1E-07
YPK_3630	*yjjU*	patatin	YPIII_S25	**2,4**	4,8E-03
YPK_3984	*yhhN*	YhhN family protein	YPIII_S25	**3,5**	2,2E-03
YPK_4129		putative transposase YhgA family protein	YPIII_S25	**2,9**	1,8E-02
YPK_4164		phage transcriptional regulator, AlpA	YPIII_S25	**5,0**	1,1E-02
YPK_4183		AsmA family protein	YPIII_S25	**2,7**	6,4E-04
YPK_4187	*yrfG-4, yigB-4, yihX-4*	HAD-superfamily hydrolase, subfamily IA, variant 3	YPIII_S25	**4,4**	2,8E-03
YPK_4212	*ravA*	regulatory ATPase RavA	YPIII_S25	**2,9**	1,5E-02
YPK_4213	*yieM*	von Willebrand factor type A	YPIII_S25	**3,5**	6,4E-03
Hypothetical					
YPK_0029		hypothetical protein YPK_0029	YPIII_E25	**4,1**	1,1E-02
YPK_0030	*yibL*	conserved hypothetical protein	YPIII_E25	**2,2**	3,1E-03
YPK_0353	*yjaG*	protein of unknown function DUF416	YPIII_E25	**2,6**	4,2E-04
YPK_0456	*yhdT*	protein of unknown function DUF997	YPIII_E25	**25,9**	2,7E-02
YPK_0828	*yggU*	protein of unknown function DUF167	YPIII_E25	**4,0**	1,4E-03
YPK_0829	*yggT*	protein of unknown function YGGT	YPIII_E25	**2,5**	4,4E-03
YPK_0830		hypothetical protein YPK_0830	YPIII_E25	**7,8**	2,4E-04
YPK_0844		hypothetical protein YPK_0844	YPIII_E25	**75,1**	7,4E-12
YPK_1059		protein of unknown function DUF446	YPIII_E25	**4,8**	2,6E-02
YPK_1170		protein of unknown function DUF969	YPIII_E25	**3,6**	1,1E-03
YPK_1295	*yfgM*	conserved hypothetical protein	YPIII_E25	**2,8**	2,3E-04
YPK_1392	*yaiI*	protein of unknown function DUF188	YPIII_E25	**19,3**	1,3E-02
YPK_1405		conserved hypothetical protein	YPIII_E25	**6,5**	2,9E-05
YPK_1516	*yfcA*	protein of unknown function DUF81	YPIII_E25	**6,7**	1,6E-03
YPK_1517	*yfcM*	protein of unknown function DUF462	YPIII_E25	**4,5**	2,7E-03
YPK_1667		conserved hypothetical protein	YPIII_E25	**5,3**	8,7E-03
YPK_1668	*yceA*	hypothetical protein	YPIII_E25	**3,1**	6,6E-04
YPK_1681	*yceD*	protein of unknown function DUF177	YPIII_E25	**13,4**	2,8E-22
YPK_1940		protein of unknown function DUF1471	YPIII_E25	**2,2**	1,6E-02
YPK_1954		conserved hypothetical protein	YPIII_E25	**34,4**	5,1E-27
YPK_2146		protein of unknown function DUF28	YPIII_E25	**8,1**	2,6E-10
YPK_2154	*yecM*	protein of unknown function DUF991	YPIII_E25	**5,4**	4,1E-06
YPK_2183		hypothetical protein YPK_2183	YPIII_E25	**4,6**	3,2E-08
YPK_2368		conserved hypothetical protein	YPIII_E25	**30,8**	2,5E-04
YPK_2379		conserved hypothetical protein	YPIII_E25	**68,8**	2,6E-05
YPK_2397		conserved hypothetical protein	YPIII_E25	**25,6**	8,0E-07
YPK_2518		conserved hypothetical protein	YPIII_E25	**127,6**	8,5E-21
YPK_2653		protein of unknown function DUF882	YPIII_E25	**2,5**	1,2E-02
YPK_2731		conserved hypothetical protein	YPIII_E25	**3,9**	6,6E-06
YPK_2781		conserved hypothetical protein	YPIII_E25	**4,7**	6,4E-06
YPK_2845		conserved hypothetical protein	YPIII_E25	**2,7**	2,7E-02
YPK_2874		protein of unknown function DUF1456	YPIII_E25	**4,7**	2,1E-04
YPK_3025	*ybeD*	protein of unknown function DUF493	YPIII_E25	**3,1**	4,1E-03
YPK_3197	*ybaB*	conserved hypothetical protein	YPIII_E25	**5,2**	9,2E-08
YPK_3236		conserved hypothetical protein	YPIII_E25	**13,2**	2,0E-14
YPK_3247	*yajQ*	protein of unknown function DUF520	YPIII_E25	**6,0**	2,8E-07
YPK_3350	*yfiH*	protein of unknown function DUF152	YPIII_E25	**3,0**	4,5E-02
YPK_3504	*yacF*	protein of unknown function DUF1342	YPIII_E25	**2,4**	1,3E-03
YPK_3580	*yjjP*	protein of unknown function DUF1212	YPIII_E25	**2,5**	2,6E-02
YPK_3753		hypothetical protein YPK_3753	YPIII_E25	**2,4**	3,9E-02
YPK_3785		conserved hypothetical protein	YPIII_E25	**43,9**	7,8E-18
YPK_3881		conserved hypothetical protein	YPIII_E25	**2,6**	2,8E-02
YPK_3882		hypothetical protein	YPIII_E25	**16,0**	2,1E-03
YPK_3883		conserved hypothetical protein	YPIII_E25	**5,1**	4,3E-03
YPK_4039		conserved hypothetical protein	YPIII_E25	**9,8**	1,8E-07
YPK_4063	*yifE*	protein of unknown function DUF413	YPIII_E25	**5,8**	3,5E-09
YPK_4193	*yihI*	protein of unknown function DUF414	YPIII_E25	**3,2**	9,0E-05
YPK_4247	*yidD*	protein of unknown function DUF37	YPIII_E25	**25,6**	9,7E-14
pYV0006		hypothetical protein	YPIII_S25	**3,9**	4,5E-03
pYV0026		hypothetical protein	YPIII_S25	**3,2**	2,8E-04
pYV0027		hypothetical protein	YPIII_S25	**3,2**	1,5E-05
YPK_0010		protein of unknown function DUF1375	YPIII_S25	**13,5**	7,7E-08
YPK_0142		conserved hypothetical protein	YPIII_S25	**5,5**	9,2E-03

Locus	Gene name	Gene description	Condition upregulated	Fold change	p-value
YPK_0166		protein of unknown function DUF1471	YPIII_S25	**26,6**	3,9E-19
YPK_0441		hypothetical protein YPK_0441	YPIII_S25	**6,4**	1,2E-02
YPK_0545		conserved hypothetical protein	YPIII_S25	**3,6**	2,1E-02
YPK_0546		conserved hypothetical protein	YPIII_S25	**2,8**	2,2E-04
YPK_0547		protein of unknown function DUF883 ElaB	YPIII_S25	**3,4**	1,2E-08
YPK_0548		protein of unknown function DUF1090	YPIII_S25	**3,8**	2,1E-05
YPK_0574		hypothetical protein YPK_0574	YPIII_S25	**27,7**	2,1E-02
YPK_0581		conserved hypothetical protein	YPIII_S25	**8,8**	2,5E-05
YPK_0597		conserved hypothetical protein	YPIII_S25	**8,9**	4,8E-02
YPK_0598		conserved hypothetical protein	YPIII_S25		1,8E-03
YPK_0631		hypothetical protein YPK_0631	YPIII_S25	**12,7**	2,2E-07
YPK_0652		conserved hypothetical protein	YPIII_S25	**2,0**	2,1E-02
YPK_0653		conserved hypothetical protein	YPIII_S25	**2,1**	3,4E-02
YPK_0691		hypothetical protein YPK_0691	YPIII_S25	**7,9**	8,7E-03
YPK_0699		conserved hypothetical protein	YPIII_S25	**2,8**	2,4E-03
YPK_0723		conserved hypothetical protein	YPIII_S25	**7,4**	4,0E-03
YPK_0732		conserved hypothetical protein	YPIII_S25	**20,6**	3,0E-07
YPK_0742		conserved hypothetical protein	YPIII_S25	**6,1**	2,2E-02
YPK_0765		conserved hypothetical protein	YPIII_S25	**16,1**	2,4E-02
YPK_0790		conserved hypothetical protein	YPIII_S25	**2,2**	1,1E-02
YPK_0870		conserved hypothetical protein	YPIII_S25	**15,6**	1,5E-11
YPK_0956		conserved hypothetical protein	YPIII_S25	**2,9**	4,9E-03
YPK_0957		conserved hypothetical protein	YPIII_S25	**12,4**	1,7E-03
YPK_0962		hypothetical protein	YPIII_S25	**8,9**	1,9E-06
YPK_1039		conserved hypothetical protein	YPIII_S25	**6,7**	7,6E-03
YPK_1056	*ygdH*	conserved hypothetical protein	YPIII_S25	**2,0**	2,1E-02
YPK_1062		conserved hypothetical protein	YPIII_S25	**2,2**	3,2E-03
YPK_1087		protein of unknown function UPF0253	YPIII_S25	**7,9**	2,3E-02
YPK_1112		hypothetical protein YPK_1112	YPIII_S25	**10,4**	1,7E-04
YPK_1130		hypothetical protein YPK_1130	YPIII_S25		3,3E-04
YPK_1160		conserved hypothetical protein	YPIII_S25	**236,2**	2,1E-13
YPK_1256		hypothetical protein YPK_1256	YPIII_S25	**7,0**	3,2E-03
YPK_1263	*yhfZ*	conserved hypothetical protein	YPIII_S25	**13,2**	2,1E-08
YPK_1320		hypothetical protein YPK_1320	YPIII_S25	**9,9**	1,9E-02
YPK_1326	*yegP*	protein of unknown function DUF1508	YPIII_S25	**47,1**	8,3E-39
YPK_1358		conserved hypothetical protein	YPIII_S25	**6,6**	4,5E-07
YPK_1359		conserved hypothetical protein	YPIII_S25	**7,3**	1,0E-02
YPK_1381		conserved hypothetical protein	YPIII_S25	**12,5**	5,2E-03
YPK_1397	*ygiW*	conserved hypothetical protein	YPIII_S25	**10,8**	3,8E-13
YPK_1398	*yfeY*	protein of unknown function DUF1131	YPIII_S25	**7,0**	3,4E-02
YPK_1445		protein of unknown function DUF1479	YPIII_S25	**10,6**	3,5E-08
YPK_1460		conserved hypothetical protein	YPIII_S25	**8,7**	6,3E-03
YPK_1491		conserved hypothetical protein	YPIII_S25	**12,2**	8,9E-03
YPK_1493		conserved hypothetical protein	YPIII_S25	**4,0**	4,9E-03
YPK_1507		conserved hypothetical protein	YPIII_S25	**2,5**	7,4E-03
YPK_1510		conserved hypothetical protein	YPIII_S25	**4,1**	1,6E-03
YPK_1574		conserved hypothetical protein	YPIII_S25	**2,5**	1,4E-02
YPK_1585	*elaB*	protein of unknown function DUF883 ElaB	YPIII_S25	**20,1**	1,6E-16
YPK_1601		protein of unknown function DUF218	YPIII_S25	**29,3**	2,4E-24
YPK_1625		hypothetical protein YPK_1625	YPIII_S25	**3,0**	3,9E-04
YPK_1626		conserved hypothetical protein	YPIII_S25	**5,3**	7,7E-04
YPK_1629		conserved hypothetical protein	YPIII_S25	**15,9**	3,2E-02
YPK_1630		conserved hypothetical protein	YPIII_S25	**8,7**	2,1E-02
YPK_1640		conserved hypothetical protein	YPIII_S25	**4,0**	9,3E-03
YPK_1657		protein of unknown function DUF6 transmembrane	YPIII_S25	**4,3**	2,1E-02
YPK_1659		conserved hypothetical protein	YPIII_S25	**6,3**	8,1E-10
YPK_1666		conserved hypothetical protein	YPIII_S25	**53,7**	3,4E-04
YPK_1673	*bssS*	conserved hypothetical protein	YPIII_S25	**25,4**	6,5E-24
YPK_1725		conserved hypothetical protein	YPIII_S25	**3,2**	2,0E-04
YPK_1729		conserved hypothetical protein	YPIII_S25	**3,2**	2,3E-04
YPK_1732		conserved hypothetical protein	YPIII_S25	**2,7**	2,3E-03
YPK_1734		hypothetical protein YPK_1734	YPIII_S25	**12,5**	4,1E-02
YPK_1762		conserved hypothetical protein	YPIII_S25	**9,5**	2,5E-03
YPK_1765		conserved hypothetical protein	YPIII_S25	**36,9**	1,6E-18
YPK_1770		conserved hypothetical protein	YPIII_S25	**13,9**	3,1E-03
YPK_1772		protein of unknown function DUF1480	YPIII_S25	**10,2**	3,5E-06
YPK_1809	*yfeE*	conserved hypothetical protein	YPIII_S25	**3,2**	1,2E-03
YPK_1810		hypothetical protein YPK_1810	YPIII_S25	**5,7**	4,1E-03
YPK_1842	*ppsR*	protein of unknown function DUF299	YPIII_S25	**8,4**	3,9E-06
YPK_1844		protein of unknown function UPF0118	YPIII_S25	**4,6**	1,9E-05
YPK_1874	*ydhL*	protein of unknown function DUF1289	YPIII_S25	**12,4**	1,3E-05
YPK_1879		conserved hypothetical protein	YPIII_S25	**23,9**	8,2E-10
YPK_1884		conserved hypothetical protein	YPIII_S25	**8,5**	1,4E-08
YPK_1885		protein of unknown function DUF1282	YPIII_S25	**213,7**	7,0E-33
YPK_1899	*ycjF*	conserved hypothetical protein	YPIII_S25	**2,5**	4,7E-03
YPK_1901		conserved hypothetical protein	YPIII_S25	**2,6**	3,2E-03
YPK_1909		hypothetical protein YPK_1909	YPIII_S25	**6,9**	1,8E-03
YPK_1910		conserved hypothetical protein	YPIII_S25	**3,2**	1,4E-02
YPK_1911		hypothetical protein YPK_1911	YPIII_S25	**7,4**	4,6E-02
YPK_1919		conserved hypothetical protein	YPIII_S25	**2,4**	9,8E-03
YPK_1921	*ydbL*	conserved hypothetical protein	YPIII_S25	**5,1**	3,0E-03
YPK_1938		conserved hypothetical protein	YPIII_S25	**45,7**	7,9E-08
YPK_1951		protein of unknown function DUF1460	YPIII_S25	**10,9**	4,6E-08
YPK_1977		protein of unknown function DUF1283	YPIII_S25	**6,9**	8,5E-05
YPK_1978		protein of unknown function DUF1161	YPIII_S25	**33,9**	1,3E-12
YPK_1989		hypothetical protein YPK_1989	YPIII_S25	**5,5**	1,8E-06
YPK_1990		conserved hypothetical protein	YPIII_S25	**7,4**	5,8E-13
YPK_2018		protein of unknown function DUF466	YPIII_S25	**14,6**	6,1E-10
YPK_2058		conserved hypothetical protein	YPIII_S25	**19,7**	7,3E-03
YPK_2059		conserved hypothetical protein	YPIII_S25	**7,8**	9,3E-07
YPK_2101		hypothetical protein YPK_2101	YPIII_S25		6,5E-08
YPK_2102	*yeaH*	protein of unknown function DUF444	YPIII_S25	**36,7**	3,1E-27
YPK_2103		protein of unknown function DUF6 transmembrane	YPIII_S25	**10,4**	2,0E-06
YPK_2150	*yecN*	conserved hypothetical protein	YPIII_S25	**6,0**	1,8E-06

Locus	Gene name	Gene description	Condition upregulated	Fold change	p-value
YPK_2185		conserved hypothetical protein	YPIII_S25	**527,2**	1,6E-70
YPK_2196		conserved hypothetical protein	YPIII_S25	**3,0**	5,1E-03
YPK_2197		conserved hypothetical protein	YPIII_S25	**5,9**	1,3E-03
YPK_2198		conserved hypothetical protein	YPIII_S25	**7,3**	1,8E-04
YPK_2199		conserved hypothetical protein	YPIII_S25	**119,6**	7,6E-07
YPK_2200		hypothetical protein YPK_2200	YPIII_S25	**832,9**	2,3E-33
YPK_2209		conserved hypothetical protein	YPIII_S25	**19,7**	2,5E-04
YPK_2219	*ydjR*	protein of unknown function DUF886	YPIII_S25	**42,0**	4,7E-13
YPK_2236		conserved hypothetical protein	YPIII_S25	**25,6**	4,5E-17
YPK_2293		conserved hypothetical protein	YPIII_S25	**8,0**	5,7E-07
YPK_2294		conserved hypothetical protein	YPIII_S25	**14,7**	7,7E-12
YPK_2295		protein of unknown function DUF497	YPIII_S25	**3,0**	8,5E-04
YPK_2309		conserved hypothetical protein	YPIII_S25	**3,2**	4,0E-03
YPK_2338		hypothetical protein YPK_2338	YPIII_S25	**8,5**	1,8E-02
YPK_2371		conserved hypothetical protein	YPIII_S25	**3,7**	2,6E-03
YPK_2372		conserved hypothetical protein	YPIII_S25	**3,6**	6,8E-04
YPK_2389		conserved hypothetical protein	YPIII_S25	**2,7**	8,0E-05
YPK_2406		conserved hypothetical protein	YPIII_S25	**2,5**	2,1E-02
YPK_2434		protein of unknown function DUF1493	YPIII_S25	**3,1**	2,1E-02
YPK_2441		conserved hypothetical protein	YPIII_S25	**71,9**	8,6E-23
YPK_2443		conserved hypothetical protein	YPIII_S25	**12,9**	6,3E-14
YPK_2444	*yqfB*	protein of unknown function DUF437	YPIII_S25	**4,8**	1,2E-08
YPK_2448	*yoaH*	protein of unknown function UPF0181	YPIII_S25	**4,0**	6,7E-05
YPK_2471		conserved hypothetical protein	YPIII_S25	**5,6**	7,5E-04
YPK_2481		conserved hypothetical protein	YPIII_S25	**5,2**	1,0E-02
YPK_2482		conserved hypothetical protein	YPIII_S25	**3,8**	1,2E-03
YPK_2483		hypothetical protein YPK_2483	YPIII_S25	**549,8**	1,0E-69
YPK_2485		conserved hypothetical protein	YPIII_S25	**8,8**	3,2E-05
YPK_2486		conserved hypothetical protein	YPIII_S25	**4,7**	1,7E-02
YPK_2507		conserved hypothetical protein	YPIII_S25	**4,1**	1,2E-03
YPK_2515		hypothetical protein	YPIII_S25	**2,2**	4,1E-02
YPK_2522		hypothetical protein YPK_2522	YPIII_S25	**15,8**	2,3E-02
YPK_2523		conserved hypothetical protein	YPIII_S25	**3,7**	2,0E-02
YPK_2555		conserved hypothetical protein	YPIII_S25	**5,4**	2,5E-04
YPK_2563	*sanA*	protein of unknown function DUF218	YPIII_S25	**2,7**	2,1E-02
YPK_2593		conserved hypothetical protein	YPIII_S25	**7,6**	1,7E-02
YPK_2604		conserved hypothetical protein	YPIII_S25	**11,7**	5,0E-02
YPK_2626		hypothetical protein	YPIII_S25	**2,8**	4,8E-02
YPK_2643		protein of unknown function DUF1379	YPIII_S25	**6,5**	1,2E-07
YPK_2654		hypothetical protein	YPIII_S25	**3,7**	5,9E-06
YPK_2663		protein of unknown function DUF1338	YPIII_S25	**47,7**	1,2E-25
YPK_2772		conserved hypothetical protein	YPIII_S25	**49,0**	6,0E-04
YPK_2785		hypothetical protein	YPIII_S25	**3,2**	2,8E-02
YPK_2790		conserved hypothetical protein	YPIII_S25	**3,3**	2,3E-03
YPK_2804		conserved hypothetical protein	YPIII_S25	**20,9**	8,2E-12
YPK_2816		conserved hypothetical protein	YPIII_S25	**12,4**	1,1E-04
YPK_2821		conserved hypothetical protein	YPIII_S25	**6,9**	2,0E-02
YPK_2879		hypothetical protein	YPIII_S25	**73,3**	1,6E-42
YPK_2880		conserved hypothetical protein	YPIII_S25	**3,1**	4,4E-03
YPK_2918	*ybhL, ybhM, yccA*	protein of unknown function UPF0005	YPIII_S25	**2,2**	6,0E-03
YPK_2984		conserved hypothetical protein	YPIII_S25	**6,0**	2,1E-02
YPK_3014		protein of unknown function DUF1451	YPIII_S25	**4,3**	1,1E-05
YPK_3034		conserved hypothetical protein	YPIII_S25	**3,0**	3,0E-02
YPK_3035		conserved hypothetical protein	YPIII_S25	**3,8**	7,6E-04
YPK_3038		conserved hypothetical protein	YPIII_S25	**5,3**	9,4E-03
YPK_3052		hypothetical protein YPK_3052	YPIII_S25	**59,1**	6,8E-04
YPK_3063		hypothetical protein YPK_3063	YPIII_S25	**31,6**	4,3E-03
YPK_3073		conserved hypothetical protein	YPIII_S25	**2,4**	1,1E-02
YPK_3086		conserved hypothetical protein	YPIII_S25	**19,9**	5,9E-03
YPK_3087		conserved hypothetical protein	YPIII_S25	**16,5**	5,7E-10
YPK_3096		hypothetical protein YPK_3096	YPIII_S25	**48,2**	1,1E-21
YPK_3097		conserved hypothetical protein	YPIII_S25	**4,5**	1,0E-09
YPK_3104		conserved hypothetical protein	YPIII_S25	**2,4**	2,8E-02
YPK_3105		hypothetical protein YPK_3105	YPIII_S25	**5,9**	1,8E-08
YPK_3106		hypothetical protein YPK_3106	YPIII_S25	**5,3**	3,1E-02
YPK_3119		hypothetical protein YPK_3119	YPIII_S25	**5,3**	2,7E-06
YPK_3162		hypothetical protein	YPIII_S25	**2,4**	1,6E-03
YPK_3203		conserved hypothetical protein	YPIII_S25	**3,9**	5,6E-06
YPK_3281	*yaiE*	protein of unknown function DUF1255	YPIII_S25	**4,2**	1,4E-06
YPK_3306	*yafK*	protein of unknown function DUF949	YPIII_S25	**2,5**	4,0E-03
YPK_3310		conserved hypothetical protein	YPIII_S25	**6,9**	6,3E-03
YPK_3423		conserved hypothetical protein	YPIII_S25	**13,8**	1,5E-04
YPK_3439		protein of unknown function UPF0150	YPIII_S25	**3,5**	1,4E-04
YPK_3486	*yacL*	conserved hypothetical protein	YPIII_S25	**3,6**	8,6E-06
YPK_3511		conserved hypothetical protein	YPIII_S25	**4,0**	5,8E-04
YPK_3528	*ygaW*	protein of unknown function DUF1144	YPIII_S25	**15,2**	7,5E-07
YPK_3567		conserved hypothetical protein	YPIII_S25	**4,6**	1,3E-06
YPK_3631		protein of unknown function DUF1328	YPIII_S25	**41,6**	1,4E-07
YPK_3644		conserved hypothetical protein	YPIII_S25	**3,1**	3,1E-02
YPK_3662		conserved hypothetical protein	YPIII_S25	**2,6**	6,2E-03
YPK_3705		conserved hypothetical protein	YPIII_S25	**6,0**	1,4E-06
YPK_3710		conserved hypothetical protein	YPIII_S25	**19,7**	1,4E-12
YPK_3711		heparinase II/III family protein	YPIII_S25	**13,5**	4,6E-09
YPK_3721		hypothetical protein YPK_3721	YPIII_S25	**3,1**	1,5E-02
YPK_3723		protein of unknown function DUF891	YPIII_S25	**2,4**	3,7E-03
YPK_3748		conserved hypothetical protein	YPIII_S25	**6,7**	2,7E-02
YPK_3773		protein of unknown function DUF1107	YPIII_S25	**61,2**	6,3E-41
YPK_3774	*ytfJ*	conserved hypothetical protein	YPIII_S25	**7,2**	7,5E-09
YPK_3780		conserved hypothetical protein	YPIII_S25	**5,0**	6,7E-05
YPK_3804		hypothetical protein	YPIII_S25	**2,0**	4,6E-02
YPK_3852		protein of unknown function DUF419	YPIII_S25	**11,6**	1,8E-10
YPK_3922		protein of unknown function DUF485	YPIII_S25	**337,9**	3,2E-26
YPK_3924	*ytaP*	conserved hypothetical protein	YPIII_S25	**4,0**	4,9E-03
YPK_3956		conserved hypothetical protein	YPIII_S25	**2,2**	4,1E-03

Locus	Gene name	Gene description	Condition upregulated	Fold change	p-value
YPK_3993		conserved hypothetical protein	YPIII_S25	**3,0**	2,3E-02
YPK_4004		conserved hypothetical protein	YPIII_S25	**2,8**	3,8E-03
YPK_4075	*yijD*	protein of unknown function DUF1422	YPIII_S25	**4,5**	1,4E-03
YPK_4107		conserved hypothetical protein	YPIII_S25	**8,1**	1,2E-04
YPK_4117		protein of unknown function DUF1454	YPIII_S25	**2,3**	1,1E-02
YPK_4208		conserved hypothetical protein	YPIII_S25	**15,1**	2,4E-06

Table S 8: List of genes that were differentially regulated by temperature. The fold change is indicated for the condition in which the gene expression was induced**.**

Locus	Gene name	Gene description	Condition upregulated	Fold change	p-vale
Virulence					
YPK_0280	*bfd*	BFD domain protein (2Fe-2S)-binding domain protein	YPIII_E25	**11,0**	2,2E-11
YPK_0792	*yspI*	autoinducer synthesis protein	YPIII_E25	**2,2**	4,3E-03
YPK_1291	*pilF*	type IV pilus biogenesis	YPIII_E25	**2,1**	2,2E-03
YPK_1449		curli production assembly/transport component CsgG	YPIII_E25	**10,5**	4,3E-06
YPK_1606	*ompX/ailD*	virulence-related outer membrane protein	YPIII_E25	**3,8**	5,9E-04
YPK_1669	*tqsA*	AI-2 transport protein TqsA	YPIII_E25	**2,5**	1,9E-02
YPK_1876	*rovA*	transcriptional regulator, MarR family	YPIII_E25	**7,9**	7,6E-11
YPK_1953	*srfB*	putative virulence factor SrfB	YPIII_E25	**37,3**	4,2E-33
YPK_2429	*invA*	invasin region 3	YPIII_E25	**17,4**	2,0E-27
pYV0001	*ypkA*	putative targeted effector protein kinase	YPIII_E37	**3,2**	3,0E-09
pYV0020	*sycH*	putative yopH targeting protein	YPIII_E37	**2,3**	2,6E-04
pYV0024	*sycE, yerA*	putative yopE chaperone	YPIII_E37	**2,2**	1,1E-02
pYV0047	*yopM*	putative targeted effector protein	YPIII_E37	**8,8**	1,1E-08
pYV0054	*yopD*	putative Yop negative regulation/targeting component	YPIII_E37	**6,3**	2,1E-18
pYV0055	*yopB*	putative Yop targeting protein	YPIII_E37	**6,9**	1,0E-05
pYV0056	*lcrH, sycD*	low calcium response protein H	YPIII_E37	**5,4**	1,1E-14
pYV0057	*lcrV*	putative V antigen, antihost protein/regulator	YPIII_E37	**3,6**	1,7E-03
pYV0058	*lcrG*	putative Yop regulator	YPIII_E37	**2,9**	1,4E-05
pYV0059	*lcrR*	hypothetical protein lcrR	YPIII_E37	**3,2**	1,5E-06
pYV0060	*lcrD, yscV*	putative membrane-bound Yop protein	YPIII_E37	**3,0**	6,5E-08
pYV0062	*yscX*	putative type III secretion protein	YPIII_E37	**2,2**	2,4E-03
pYV0063	*sycN*	putative type III secretion protein	YPIII_E37	**2,7**	2,2E-05
pYV0064	*tyeA*	putative Yop secretion and targeting protein	YPIII_E37	**2,6**	4,8E-05
pYV0065	*yopN, lcrE*	putative membrane-bound Yop targeting protein	YPIII_E37	**2,4**	3,0E-05
pYV0068	*yscO*	putative type III secretion protein	YPIII_E37	**2,0**	5,0E-03
pYV0069	*yscP*	putative type III secretion protein	YPIII_E37	**2,2**	4,8E-05
pYV0070	*yscQ*	putative type III secretion protein	YPIII_E37	**4,3**	4,0E-10
pYV0071	*yscR*	putative Yop secretion membrane protein	YPIII_E37	**3,4**	2,2E-06
pYV0072	*yscS*	putative type III secretion protein	YPIII_E37	**2,3**	8,0E-03
pYV0073	*yscT*	putative type III secretion protein	YPIII_E37	**3,6**	1,4E-07
pYV0074	*yscU*	putative type III secretion protein	YPIII_E37	**7,5**	1,5E-17
pYV0075	*virG*	putative Yop targeting lipoprotein	YPIII_E37	**4,0**	8,9E-03
pYV0076	*lcrF, virF*	putative thermoregulatory protein	YPIII_E37	**6,2**	8,6E-07
pYV0079	*yscC*	putative type III secretion protein	YPIII_E37	**2,0**	1,1E-02
pYV0081	*yscE*	putative type III secretion protein	YPIII_E37	**3,6**	4,4E-05
pYV0082	*yscF*	putative type III secretion protein	YPIII_E37	**2,8**	3,7E-04
pYV0083	*yscG*	putative type III secretion protein	YPIII_E37	**3,1**	3,4E-07
pYV0084	*yscH*	yscH, yopR, lcrP; putative type III secretion protein	YPIII_E37	**3,0**	4,2E-07
pYV0085	*yscI, lcrO*	putative type III secretion protein	YPIII_E37	**3,8**	4,7E-10
pYV0086	*yscJ, ylpB*	putative type III secretion lipoprotein	YPIII_E37	**4,0**	7,8E-05
pYV0087	*yscK*	putative type III secretion protein	YPIII_E37	**3,3**	3,4E-08
pYV0088	*yscL*	putative type III secretion protein	YPIII_E37	**6,8**	5,1E-13
pYV0089	*yscM, lcrQ*	putative type III secretion regulatory	YPIII_E37	**12,3**	2,8E-10
pYV0094	*yopH*	putative protein-tyrosine phosphatase Yop effector	YPIII_E37	**3,2**	2,1E-09
pYV0098	*yopP, yopJ*	putative targeted effector protein	YPIII_E37	**5,5**	6,1E-04
YPK_0386	*impB*	type VI secretion protein, VC_A0107 family	YPIII_E37	**4,6**	4,6E-02
YPK_0389	*impG-1, vasA-1*	type VI secretion protein, VC_A0110 family	YPIII_E37	**2,4**	4,6E-02
YPK_0575	*fhaB-3*	putative adhesin	YPIII_E37	**4,8**	2,2E-06
YPK_0577	*fhaB-1*	putative adhesin	YPIII_E37	**3,7**	1,0E-02
YPK_0582	*fhaB-2*	putative adhesin/hemolysin	YPIII_E37	**3,0**	2,8E-02
YPK_0696	*papD*	pili assembly chaperone	YPIII_E37	**3,6**	4,3E-02
YPK_0697		fimbrial protein	YPIII_E37	**5,4**	1,1E-02
YPK_1268	*ailA*	virulence-related outer membrane protein	YPIII_E37	**4,3**	4,1E-13
YPK_1315	*yeeJ*	Ig domain protein group 1 domain protein	YPIII_E37	**3,1**	1,5E-02
YPK_1559	*rovM*	transcriptional regulator, LysR family	YPIII_E37	**2,8**	1,1E-02
YPK_1705	*ycfJ*	17 kDa surface antigen	YPIII_E37	**5,4**	5,3E-13
YPK_2615	*cnfy*	cytotoxic necrotizing factor	YPIII_E37	**7,2**	3,6E-05
YPK_2759	*psaA*	pH 6 antigen precursor (antigen 4) (adhesin)	YPIII_E37	**4,9**	4,2E-02
YPK_2826		type III effector Hrp-dependent outers	YPIII_E37	**2,5**	3,0E-02
YPK_3653	*lsrB*	autoinducer AI-2 ABC transporter, periplasmic AI-2-binding protein	YPIII_E37	**59,8**	5,2E-18
Cell motility and chemotaxis					
YPK_0034	*tar*	methyl-accepting chemotaxis sensory transducer	YPIII_E25	**91,3**	4,3E-21
YPK_1745	*flhD*	flagellar transcriptional activator	YPIII_E25	**2,6**	2,1E-04
YPK_1746	*flhC*	flagellar transcriptional activator FlhC	YPIII_E25	**2,8**	4,4E-07
YPK_1747	*motA*	chemotaxis protein MotA	YPIII_E25	**7,5**	1,4E-11
YPK_1748	*motB*	OmpA/MotB domain protein	YPIII_E25	**6,9**	1,1E-13
YPK_1749	*cheA*	CheA signal transduction histidine kinase	YPIII_E25	**7,3**	2,2E-17
YPK_1750	*cheW*	CheW protein	YPIII_E25	**8,5**	4,5E-13
YPK_1753	*cheD*	methyl-accepting chemotaxis sensory transducer	YPIII_E25	**168,6**	1,0E-51
YPK_1756	*cheR*	MCP methyltransferase, CheR-type	YPIII_E25	**16,7**	4,9E-16
YPK_1757	*cheB*	response regulator receiver modulated CheB methylesterase	YPIII_E25	**46,9**	1,4E-18
YPK_1758	*cheY*	response regulator receiver protein	YPIII_E25	**11,1**	2,8E-12

Locus	Gene name	Gene description	Condition upregulated	Fold change	p-vale
YPK_1759	*cheZ*	chemotaxis phosphatase, CheZ	YPIII_E25	**15,7**	1,4E-16
YPK_2378	*fliZ*	flagella biosynthesis protein FliZ	YPIII_E25	**30,1**	3,7E-28
YPK_2380	*fliA*	RNA polymerase, sigma 28 subunit, FliA/WhiG	YPIII_E25	**57,5**	9,7E-42
YPK_2381	*fliC*	flagellin domain protein	YPIII_E25	**608,6**	8,5E-100
YPK_2382	*fliD*	flagellar hook-associated 2 domain protein	YPIII_E25	**66,2**	1,1E-46
YPK_2383	*fliS*	flagellar protein FliS	YPIII_E25	**53,2**	2,2E-26
YPK_2384	*fliT*	flagellar export chaperone	YPIII_E25	**98,7**	5,8E-23
YPK_2386		chemotactic transducer-related protein	YPIII_E25	**3,3**	3,6E-02
YPK_2390	*fliE*	flagellar hook-basal body complex subunit FliE	YPIII_E25	**99,3**	1,0E-15
YPK_2391	*fliF*	flagellar M-ring protein FliF	YPIII_E25	**86,7**	9,4E-47
YPK_2392	*fliG*	flagellar motor switch protein FliG	YPIII_E25	**34,7**	1,9E-32
YPK_2393	*fliH*	flagellar assembly protein FliH	YPIII_E25	**41,7**	4,8E-23
YPK_2394	*fliI*	ATPase, FliI/YscN family	YPIII_E25	**54,8**	5,7E-24
YPK_2395	*fliJ*	flagellar export protein FliJ	YPIII_E25	**57,9**	8,7E-19
YPK_2396	*fliK-1*	flagellar hook-length control protein	YPIII_E25	**26,9**	7,5E-14
YPK_2398	*fliL*	flagellar basal body-associated protein FliL	YPIII_E25	**307,6**	1,8E-40
YPK_2399	*fliM*	flagellar motor switch protein FliM	YPIII_E25	**86,3**	7,2E-35
YPK_2400	*fliN*	flagellar motor switch protein FliN	YPIII_E25	**55,0**	2,0E-24
YPK_2401	*fliO*	flagellar biosynthesis protein FliO	YPIII_E25	**366,8**	7,1E-25
YPK_2402	*fliP*	flagellar biosynthetic protein FliP	YPIII_E25	**142,9**	1,8E-23
YPK_2403	*fliQ*	flagellar biosynthetic protein FliQ	YPIII_E25	**85,6**	3,2E-04
YPK_2404	*fliR*	flagellar biosynthetic protein FliR	YPIII_E25		1,6E-08
YPK_2415	*flgL*	flagellar hook-associated protein 3	YPIII_E25	**38,3**	5,7E-38
YPK_2416	*flgK*	flagellar hook-associated protein FlgK	YPIII_E25	**84,3**	3,0E-46
YPK_2417	*flgJ*	flagellar rod assembly protein/muramidase FlgJ	YPIII_E25	**38,6**	2,2E-22
YPK_2418	*flgI*	flagellar P-ring protein	YPIII_E25	**35,8**	8,6E-22
YPK_2419	*flgH*	flagellar L-ring protein	YPIII_E25	**66,8**	5,1E-20
YPK_2420	*flgG*	flagellar basal-body rod protein FlgG	YPIII_E25	**150,8**	8,7E-46
YPK_2421	*flgF*	flagellar basal-body rod protein FlgF	YPIII_E25	**161,7**	7,4E-40
YPK_2422	*flgE*	flagellar basal body FlaE domain protein	YPIII_E25	**96,3**	2,6E-58
YPK_2423	*flgD*	flagellar hook capping protein	YPIII_E25	**93,8**	2,2E-43
YPK_2424	*flgC*	flagellar basal-body rod protein FlgC	YPIII_E25	**59,2**	1,7E-36
YPK_2425	*flgB*	flagellar basal-body rod protein FlgB	YPIII_E25	**129,0**	6,8E-52
YPK_2426	*flgA*	flagella basal body P-ring formation protein FlgA	YPIII_E25	**59,0**	2,3E-22
YPK_2427	*flgM*	anti-sigma-28 factor, FlgM	YPIII_E25	**19,1**	2,5E-14
YPK_2428	*flgN*	FlgN family protein	YPIII_E25	**12,8**	5,8E-16
YPK_2430	*flhE*	flagellar FlhE family protein	YPIII_E25	**25,2**	8,0E-06
YPK_2431	*flhA*	flagellar biosynthesis protein FlhA	YPIII_E25	**35,9**	4,1E-27
YPK_2432	*flhB*	flagellar biosynthetic protein FlhB	YPIII_E25	**43,6**	4,2E-20
YPK_2833	*tsr2*	methyl-accepting chemotaxis sensory transducer with Cache sensor	YPIII_E25	**16,6**	1,4E-11
YPK_3286		YcgR family protein	YPIII_E25	**4,3**	6,5E-04
YPK_3617		OmpA/MotB domain protein	YPIII_E25	**3,1**	3,7E-02
Stress adaptation					
YPK_0011	*ibpA*	heat shock protein Hsp20	YPIII_E25	**4,2**	2,7E-06
YPK_0012	*ibpB*	heat shock protein Hsp20	YPIII_E25	**3,9**	2,9E-04
YPK_0035	*sodA*	superoxide dismutase	YPIII_E25	**2,2**	4,7E-05
YPK_0175	*hslO*	Hsp33 protein	YPIII_E25	**2,1**	2,5E-03
YPK_0444	*cspA-3*	cold-shock DNA-binding domain protein	YPIII_E25	**5,8**	2,9E-03
YPK_1124	*cspB-1*	cold-shock DNA-binding domain protein	YPIII_E25	**11,0**	4,9E-05
YPK_1740	*cspC-1*	cold-shock DNA-binding domain protein	YPIII_E25	**20,2**	6,8E-15
YPK_2621	*hspQ*	heat shock protein HspQ	YPIII_E25	**2,4**	2,3E-04
YPK_2662	*cspB-2*	cold-shock DNA-binding domain protein	YPIII_E25	**12,0**	3,0E-13
YPK_3161	*ybbN*	thioredoxin domain	YPIII_E25	**2,3**	4,0E-04
YPK_4080		glutaredoxin-family domain protein	YPIII_E25	**2,7**	1,9E-02
YPK_0120	*uspA*	UspA domain protein	YPIII_E37	**2,8**	6,2E-07
YPK_0564	*hdeD*	acid-resistance membrane protein	YPIII_E37	**3,3**	1,4E-08
YPK_1140	*hdeB*	acid-resistance protein	YPIII_E37	**2,8**	4,0E-05
YPK_1863	*sodB*	superoxide dismutase	YPIII_E37	**4,3**	9,2E-10
YPK_1883	*gst*	glutathione S-transferase domain	YPIII_E37	**3,8**	5,9E-06
YPK_2694	*cspD-2*	cold-shock DNA-binding domain protein	YPIII_E37	**3,4**	4,2E-06
YPK_2855	*katA*	catalase	YPIII_E37	**11,0**	3,0E-04
YPK_3388	*katY*	catalase/peroxidase HPI	YPIII_E37	**49,4**	4,7E-35
YPK_3445	*sodC*	superoxide dismutase	YPIII_E37	**6,8**	1,1E-19
YPK_3822	*groEL*	chaperonin GroEL	YPIII_E37	**3,0**	3,8E-09
YPK_3823	*groES*	chaperonin Cpn10	YPIII_E37	**2,8**	4,9E-08
Information storage and processing					
Replication, cell division					
YPK_0635	*dnaG*	DNA primase	YPIII_E25	**2,5**	2,5E-06
YPK_1108	*rnhA*	ribonuclease H	YPIII_E25	**3,0**	4,0E-02
YPK_2033	*topA*	DNA topoisomerase I	YPIII_E25	**2,1**	2,6E-04
YPK_2145	*ruvC*	crossover junction endodeoxyribonuclease RuvC	YPIII_E25	**4,1**	1,4E-07
YPK_2617		transposase	YPIII_E25	**8,0**	2,0E-02
YPK_2898	*rhlE*	DEAD/DEAH box helicase domain protein	YPIII_E25	**3,1**	1,5E-05
YPK_3676		integrase family protein	YPIII_E25	**3,4**	3,5E-05
YPK_3783	*priB*	primosomal replication protein N	YPIII_E25	**4,4**	2,4E-12
YPK_4036	*rhlB*	DEAD/DEAH box helicase domain protein	YPIII_E25	**2,0**	1,1E-03
YPK_4152	*mutM*	formamidopyrimidine-DNA glycosylase	YPIII_E25	**4,8**	6,2E-05
YPK_4155	*radC*	DNA repair protein RadC	YPIII_E25	**2,7**	3,4E-06
pYV0090		putative transposase	YPIII_E37	**19,4**	1,2E-07
pYV0091		putative transposase	YPIII_E37	**14,4**	8,7E-04
pYV0092		putative transposase	YPIII_E37	**9,8**	5,4E-03
YPK_0061		integrase family protein	YPIII_E37	**2,2**	1,5E-02
YPK_0106	*yhjD*	ribonuclease	YPIII_E37	**2,7**	1,5E-02
YPK_1043	*recB*	exodeoxyribonuclease V, beta subunit	YPIII_E37	**2,7**	3,5E-06
YPK_1044	*recD*	exodeoxyribonuclease V, alpha subunit	YPIII_E37	**2,8**	4,1E-04
YPK_1542	*yfcH*	cell division inhibitor	YPIII_E37	**3,5**	9,6E-04
YPK_1984	*tus*	DNA replication terminus site-binding protein	YPIII_E37	**4,7**	1,7E-03
YPK_2439	*holE*	DNA polymerase II beta subunit	YPIII_E37	**3,3**	4,4E-03
YPK_3149		integrase family protein	YPIII_E37	**2,4**	9,6E-04
General transcription, transcription factors, signal transduction					
YPK_0103		diguanylate phosphodiesterase	YPIII_E25	**17,0**	1,2E-13

Locus	Gene name	Gene description	Condition upregulated	Fold change	p-vale
YPK_0308	*rpoA*	DNA-directed RNA polymerase, alpha subunit	YPIII_E25	**2,8**	9,2E-08
YPK_0334	*nusG*	NusG antitermination factor	YPIII_E25	**2,2**	1,1E-04
YPK_0341	*rpoC*	DNA-directed RNA polymerase, beta' subunit	YPIII_E25	**2,2**	5,9E-05
YPK_0452	*fis*	transcriptional regulator, Fis family	YPIII_E25	**6,2**	2,6E-09
YPK_0493	*rnk*	GreA/GreB family elongation factor	YPIII_E25	**2,3**	9,7E-04
YPK_0837	*algH*	putative transcriptional regulator	YPIII_E25	**2,6**	5,6E-04
YPK_1384	*narP*	two component transcriptional regulator, LuxR family	YPIII_E25	**5,7**	3,2E-06
YPK_1671	*csgD*	transcriptional regulator, LuxR family	YPIII_E25	**4,9**	2,2E-02
YPK_2074	*hns*	histone family protein nucleoid-structuring protein H-NS	YPIII_E25	**2,2**	2,8E-05
YPK_2269	*fimZ*	two component transcriptional regulator, LuxR family	YPIII_E25	**2,0**	1,9E-02
YPK_2385		transcriptional regulator, AraC family	YPIII_E25	**45,2**	1,6E-14
YPK_2499	*uhpA*	two component transcriptional regulator, LuxR family	YPIII_E25	**2,9**	7,5E-03
YPK_2686	*lrp*	transcriptional regulator, AsnC family	YPIII_E25	**2,7**	1,1E-04
YPK_3492	*pdhR*	GntR domain protein	YPIII_E25	**2,8**	3,1E-06
YPK_3547	*rapA*	SNF2-related protein	YPIII_E25	**4,3**	3,9E-11
YPK_3616		diguanylate cyclase	YPIII_E25	**4,0**	6,2E-03
YPK_3731	*nusA*	NusA antitermination factor	YPIII_E25	**2,3**	3,4E-05
YPK_3739	*greA*	transcription elongation factor GreA	YPIII_E25	**2,2**	1,3E-03
YPK_3762	*argR*	arginine repressor, ArgR	YPIII_E25	**2,9**	2,5E-04
YPK_4178	*spoT*	(p)ppGpp synthetase I, SpoT/RelA	YPIII_E25	**2,2**	1,1E-04
YPK_4190	*glnL*	signal transduction histidine kinase, nitrogen specific, NtrB	YPIII_E25	**2,4**	2,0E-02
YPK_0160	*malT*	ATP-dependent transcriptional regulator, MalT-like, LuxR family	YPIII_E37	**2,0**	7,2E-04
YPK_0173	*envZ*	integral membrane sensor signal transduction histidine kinase	YPIII_E37	**2,2**	2,0E-05
YPK_0367	*iclR*	transcriptional regulator, IclR family	YPIII_E37	**3,1**	1,3E-02
YPK_0533	*arcB*	multi-sensor hybrid histidine kinase	YPIII_E37	**2,1**	1,5E-03
YPK_0976	*lacI*	transcriptional regulator, LacI family	YPIII_E37	**2,9**	2,1E-03
YPK_1086		transcriptional antiterminator, Rof	YPIII_E37	**2,2**	1,9E-03
YPK_1182	*rpoE*	RNA polymerase, sigma-24 subunit, ECF subfamily	YPIII_E37	**3,0**	1,9E-07
YPK_1183	*rseA*	anti sigma-E protein, RseA	YPIII_E37	**5,0**	5,5E-13
YPK_1184	*rseB*	sigma E regulatory protein, MucB/RseB	YPIII_E37	**7,4**	1,2E-16
YPK_1185	*rseC*	positive regulator of sigma E, RseC/MucC	YPIII_E37	**6,2**	1,3E-05
YPK_1270	*csiE*	stationary phase inducible protein CsiE	YPIII_E37	**6,0**	1,8E-04
YPK_1328	*baeS*	integral membrane sensor signal transduction histidine kinase	YPIII_E37	**3,0**	1,9E-02
YPK_1549		transcriptional regulator, LacI family	YPIII_E37	**4,6**	7,9E-05
YPK_1614	*lacI, galR*	transcriptional regulator, LacI family	YPIII_E37	**2,1**	2,4E-02
YPK_1615	*dmlR*	transcriptional regulator, LysR family	YPIII_E37	**6,6**	2,6E-04
YPK_1715	*phoP*	two component transcriptional regulator, winged helix family	YPIII_E37	**2,7**	1,6E-03
YPK_1733	*lrp*	transcriptional regulator, AsnC family	YPIII_E37	**2,7**	1,2E-02
YPK_1936	*rstB*	integral membrane sensor signal transduction histidine kinase	YPIII_E37	**2,2**	4,9E-02
YPK_1943	*uspE*	UspA domain protein	YPIII_E37	**2,1**	1,8E-03
YPK_1975		GAF modulated sigma54 specific transcriptional regulator, Fis family	YPIII_E37	**7,0**	7,6E-12
YPK_2078	*rssB*	response regulator receiver protein	YPIII_E37	**4,6**	4,4E-02
YPK_2100	*prkA*	putative serine protein kinase, PrkA	YPIII_E37	**2,8**	9,0E-03
YPK_2166		ROK family protein	YPIII_E37	**2,4**	1,3E-02
YPK_2231		putative transcriptional regulator, GntR family	YPIII_E37	**3,3**	7,4E-04
YPK_2235	*phoH*	PhoH family protein	YPIII_E37	**7,6**	5,0E-09
YPK_2414		transcriptional regulator, DeoR family	YPIII_E37	**2,1**	2,1E-02
YPK_2491	*thuR*	transcriptional regulator, LacI family	YPIII_E37	**3,8**	3,3E-05
YPK_3206	*acrR*	transcriptional regulator, TetR family	YPIII_E37	**3,3**	4,4E-03
YPK_3397	*fucR*	transcriptional regulator, DeoR family	YPIII_E37	**17,4**	5,0E-05
YPK_3417		transcriptional regulator, DeoR family	YPIII_E37	**3,1**	2,4E-06
YPK_3425	*rpoS*	RNA polymerase, sigma 70 subunit, RpoD family	YPIII_E37	**2,6**	4,6E-06
YPK_3649	*ydeW*	transcriptional regulator, DeoR family	YPIII_E37	**3,4**	6,2E-05
YPK_3713	*yhbS*	GCN5-related N-acetyltransferase	YPIII_E37	**2,2**	7,2E-04
YPK_3841	*rhaR*	transcriptional regulator, AraC family	YPIII_E37	**4,7**	2,1E-07
YPK_3842	*rhaS*	transcriptional regulator, AraC family	YPIII_E37	**3,3**	3,9E-02
YPK_4006		transcriptional regulator, TetR family	YPIII_E37	**7,2**	2,8E-12
YPK_4101	*cytR*	transcriptional regulator, LacI family	YPIII_E37	**2,1**	1,2E-02
Translation					
YPK_0176	*hslR*	RNA-binding S4 domain protein	YPIII_E25	**2,3**	1,9E-03
YPK_0275	*rpsL*	30S ribosomal protein S12	YPIII_E25	**2,5**	8,7E-06
YPK_0276	*rpsG*	ribosomal protein S7	YPIII_E25	**2,4**	7,3E-06
YPK_0277	*fusA*	translation elongation factor G	YPIII_E25	**2,1**	2,8E-04
YPK_0282	*rpsJ*	ribosomal protein S10	YPIII_E25	**2,7**	6,9E-07
YPK_0283	*rplC*	ribosomal protein L3	YPIII_E25	**2,9**	2,0E-04
YPK_0284	*rplD*	ribosomal protein L4/L1e	YPIII_E25	**3,5**	8,9E-10
YPK_0285	*rplW*	ribosomal protein L25/L23	YPIII_E25	**2,7**	5,8E-03
YPK_0286	*rplB*	ribosomal protein L2	YPIII_E25	**3,0**	1,7E-08
YPK_0287	*rpsS*	ribosomal protein S19	YPIII_E25	**3,2**	5,8E-08
YPK_0288	*rplV*	ribosomal protein L22	YPIII_E25	**2,2**	1,1E-02
YPK_0289	*rpsC*	ribosomal protein S3	YPIII_E25	**3,1**	1,2E-08
YPK_0290	*rplP*	ribosomal protein L16	YPIII_E25	**2,8**	2,7E-04
YPK_0291	*rpmC*	ribosomal protein L29	YPIII_E25	**2,7**	1,0E-02
YPK_0292	*rpsQ*	ribosomal protein S17	YPIII_E25	**3,4**	2,4E-08
YPK_0293	*rplN*	ribosomal protein L14	YPIII_E25	**2,5**	4,2E-05
YPK_0294	*rplX*	ribosomal protein L24	YPIII_E25	**3,0**	5,7E-08
YPK_0295	*rplE*	ribosomal protein L5	YPIII_E25	**2,7**	7,3E-07
YPK_0296	*rpsN*	ribosomal protein S14	YPIII_E25	**2,7**	1,3E-06
YPK_0297	*rpsH*	ribosomal protein S8	YPIII_E25	**2,7**	7,4E-07
YPK_0298	*rplF*	ribosomal protein L6	YPIII_E25	**2,6**	2,8E-06
YPK_0299	*rplR*	ribosomal protein L18	YPIII_E25	**3,0**	5,0E-08
YPK_0300	*rpsE*	ribosomal protein S5	YPIII_E25	**3,1**	1,6E-08
YPK_0301	*rpmD*	ribosomal protein L30	YPIII_E25	**3,1**	2,5E-08
YPK_0302	*rplO*	ribosomal protein L15	YPIII_E25	**3,2**	2,6E-08
YPK_0304	*rpmJ*	ribosomal protein L36	YPIII_E25	**3,8**	1,5E-10
YPK_0305	*rpsM*	ribosomal protein S13	YPIII_E25	**2,4**	4,4E-06
YPK_0306	*rpsK*	ribosomal protein S11	YPIII_E25	**3,0**	1,5E-05
YPK_0307	*rpsD*	ribosomal protein S4	YPIII_E25	**2,5**	2,3E-06
YPK_0309	*rplQ*	ribosomal protein L17	YPIII_E25	**2,8**	2,6E-07
YPK_0335	*rplK*	ribosomal protein L11	YPIII_E25	**2,9**	8,5E-08
YPK_0336	*rplA*	ribosomal protein L1	YPIII_E25	**2,9**	6,0E-08
YPK_0337	*rplJ*	ribosomal protein L10	YPIII_E25	**3,0**	1,9E-08
YPK_0338	*rplL*	ribosomal protein L7/L12	YPIII_E25	**3,3**	2,3E-03

Locus	Gene name	Gene description	Condition upregulated	Fold change	p-vale
YPK_0453	*dusB*	TIM-barrel protein, nifR3 family	YPIII_E25	**7,0**	1,2E-20
YPK_0524	*rplM*	ribosomal protein L13	YPIII_E25	**2,9**	1,8E-07
YPK_0525	*rpsI*	ribosomal protein S9	YPIII_E25	**2,5**	2,9E-06
YPK_0636	*rpsU*	ribosomal protein S21	YPIII_E25	**3,3**	2,0E-09
YPK_1066	*rpsB*	ribosomal protein S2	YPIII_E25	**2,3**	3,3E-05
YPK_1297	*engA*	small GTP-binding protein	YPIII_E25	**2,1**	2,9E-04
YPK_1682	*rpmF*	ribosomal protein L32	YPIII_E25	**2,9**	5,4E-07
YPK_1821	*infC*	initiation factor 3	YPIII_E25	**2,0**	2,5E-04
YPK_1822	*rpmI*	ribosomal protein L35	YPIII_E25	**3,3**	3,3E-08
YPK_1823	*rplT*	ribosomal protein L20	YPIII_E25	**2,6**	1,2E-06
YPK_1824	*pheS*	phenylalanyl-tRNA synthetase, alpha subunit	YPIII_E25	**2,1**	1,1E-04
YPK_2039	*rluB*	23S rRNA pseudouridylate synthase B	YPIII_E25	**2,2**	5,1E-04
YPK_2040	*rimN*	tRNA threonylcarbamoyladenosine biosynthesis protein	YPIII_E25	**2,3**	6,0E-03
YPK_2148	*aspS*	aspartyl-tRNA synthetase	YPIII_E25	**2,9**	1,7E-07
YPK_2668	*rpsA*	ribosomal protein S1	YPIII_E25	**2,0**	2,8E-04
YPK_2725	*rumB*	23S rRNA (uracil-5-)-methyltransferase RumB	YPIII_E25	**2,1**	3,6E-02
YPK_3265	*queA*	S-adenosylmethionine--tRNA-ribosyltransferase-isomerase	YPIII_E25	**2,3**	1,0E-03
YPK_3340	*yfiF*	tRNA/rRNA methyltransferase (SpoU)	YPIII_E25	**2,3**	4,8E-05
YPK_3351	*rluD*	pseudouridine synthase, RluA family	YPIII_E25	**2,7**	2,4E-04
YPK_3361	*rplS*	ribosomal protein L19	YPIII_E25	**3,0**	1,6E-08
YPK_3362	*trmD*	tRNA (guanine-N1)-methyltransferase	YPIII_E25	**3,5**	4,3E-10
YPK_3363	*rimM*	16S rRNA processing protein RimM	YPIII_E25	**3,8**	9,6E-11
YPK_3364	*rpsP*	ribosomal protein S16	YPIII_E25	**3,5**	1,7E-10
YPK_3590	*rpsT*	ribosomal protein S20	YPIII_E25	**3,1**	2,4E-09
YPK_3724	*deaD*	DEAD/DEAH box helicase domain protein	YPIII_E25	**2,2**	1,0E-03
YPK_3726	*pnp*	polyribonucleotide nucleotidyltransferase	YPIII_E25	**2,0**	6,3E-04
YPK_3727	*rpsO*	ribosomal protein S15	YPIII_E25	**2,4**	9,4E-06
YPK_3728	*truB*	tRNA pseudouridine synthase B	YPIII_E25	**2,7**	7,4E-06
YPK_3729	*rbfA*	ribosome-binding factor A	YPIII_E25	**2,6**	1,8E-05
YPK_3737	*rrmJ*	ribosomal RNA large subunit methyltransferase J	YPIII_E25	**4,4**	7,7E-09
YPK_3738	*yhbY*	RNA-binding protein	YPIII_E25	**2,8**	9,1E-04
YPK_3743	*obgE*	GTP-binding protein Obg/CgtA	YPIII_E25	**2,5**	1,7E-05
YPK_3756	*rpmA*	ribosomal protein L27	YPIII_E25	**3,0**	8,6E-09
YPK_3757	*rplU*	ribosomal protein L21	YPIII_E25	**2,1**	3,0E-02
YPK_3781	*rplI*	ribosomal protein L9	YPIII_E25	**4,6**	2,9E-13
YPK_3782	*rpsR*	ribosomal protein S18	YPIII_E25	**4,8**	2,7E-14
YPK_3784	*rpsF*	ribosomal protein S6	YPIII_E25	**4,5**	8,6E-11
YPK_3812	*poxA*	lysyl-tRNA synthetase-related protein GenX	YPIII_E25	**2,3**	3,3E-04
YPK_4098	*rpmE*	ribosomal protein L31	YPIII_E25	**2,6**	1,3E-06
YPK_4135	*trmL, cspR*	RNA methyltransferase, TrmH family, group 2	YPIII_E25	**6,0**	1,8E-05
YPK_4153	*rpmG*	ribosomal protein L33	YPIII_E25	**3,2**	3,2E-02
YPK_4154	*rpmB*	ribosomal protein L28	YPIII_E25	**3,6**	3,0E-11
YPK_4188	*bipA*	GTP-binding protein TypA	YPIII_E25	**2,3**	4,5E-05
YPK_4248	*rnpA*	ribonuclease P protein component	YPIII_E25	**2,7**	1,3E-06
YPK_4249	*rpmH*	ribosomal protein L34	YPIII_E25	**3,0**	4,8E-08
YPK_0149	*glgC*	glucose-1-phosphate adenylyltransferase	YPIII_E37	**2,9**	3,3E-04
YPK_0504	*yhbH*	sigma 54 modulation protein/ribosomal protein S30EA	YPIII_E37	**2,5**	3,0E-03
YPK_0604		endoribonuclease L-PSP	YPIII_E37	**4,3**	1,0E-02
YPK_1060	*truC*	tRNA pseudouridine synthase C	YPIII_E37	**2,0**	2,5E-03
YPK_3353	*yfiA*	sigma 54 modulation protein/ribosomal protein S30EA	YPIII_E37	**3,7**	8,7E-12
YPK_3435	*cysN*	sulfate adenylyltransferase, large subunit	YPIII_E37	**6,7**	7,2E-04
Posttranslational modification, protein turnover					
YPK_1340	*yegD*	putative chaperone protein	YPIII_E25	**13,7**	2,8E-19
YPK_1847	*sufA*	FeS assembly scaffold SufA	YPIII_E25	**3,1**	2,5E-05
YPK_1848	*sufB*	FeS assembly protein SufB	YPIII_E25	**3,0**	9,1E-07
YPK_1849	*sufC*	FeS assembly ATPase SufC	YPIII_E25	**2,0**	1,7E-03
YPK_1850	*sufD*	FeS assembly protein SufD	YPIII_E25	**2,5**	6,7E-05
YPK_1851	*sufS*	cysteine desulfurase, SufS subfamily	YPIII_E25	**2,6**	6,7E-05
YPK_1852	*sufE*	cysteine desulfuration protein SufE	YPIII_E25	**3,2**	1,3E-03
YPK_2111	*dsbB*	disulphide bond formation protein DsbB	YPIII_E25	**2,6**	2,3E-04
YPK_2620	*rlmI*	23S rRNA (cytosine1962-C5)-methyltransferase	YPIII_E25	**2,7**	1,3E-05
YPK_2675	*ycaO*	ribosomal protein S12 methylthiotransferase	YPIII_E25	**5,7**	1,5E-14
YPK_3235	*tig*	trigger factor	YPIII_E25	**2,4**	2,4E-06
YPK_3732	*rimP*	ribosome maturation factor RimP	YPIII_E25	**3,0**	3,7E-07
YPK_3986	*tusA, sirA*	SirA family protein	YPIII_E25	**3,6**	5,0E-03
YPK_4040	*ppiC*	PpiC-type peptidyl-prolyl cis-trans isomerase	YPIII_E25	**3,1**	1,4E-02
YPK_4103	*hslV*	20S proteasome A and B subunits	YPIII_E25	**3,0**	8,0E-06
YPK_1042	*ptrA*	peptidase M16 domain protein	YPIII_E37	**3,9**	3,5E-10
YPK_1134	*ureE*	UreE urease accessory domain protein	YPIII_E37	**9,5**	2,6E-15
YPK_1135	*ureF*	urease accessory protein UreF	YPIII_E37	**10,5**	1,6E-05
YPK_1137	*ureD*	urease accessory protein UreD	YPIII_E37	**3,3**	3,5E-05
YPK_1172	*pcp*	pyrrolidone-carboxylate peptidase	YPIII_E37	**2,6**	5,0E-06
YPK_1356		peptidase M48 Ste24p	YPIII_E37	**3,0**	6,3E-06
YPK_2095	*msrB*	methionine-R-sulfoxide reductase	YPIII_E37	**2,5**	9,0E-05
YPK_3444	*ygcF*	radical SAM domain protein	YPIII_E37	**2,6**	5,1E-06
YPK_3452	*htrA*	protease Do	YPIII_E37	**7,5**	7,0E-20
YPK_3715	*ydcP-2, yegQ-2, yhbU-2*	peptidase U32	YPIII_E37	**2,2**	4,2E-02
Metabolism					
Energy production and conversion					
YPK_0152	*glpD*	FAD dependent oxidoreductase	YPIII_E25	**40,1**	8,7E-50
YPK_1550	*pta*	phosphate acetyltransferase	YPIII_E25	**3,8**	4,4E-11
YPK_1551	*ackA*	acetate kinase	YPIII_E25	**3,2**	4,9E-08
YPK_1702	*ndh*	FAD-dependent pyridine nucleotide-disulphide oxidoreductase	YPIII_E25	**3,4**	1,8E-06
YPK_2072	*adhE*	iron-containing alcohol dehydrogenase	YPIII_E25	**16,0**	1,9E-37
YPK_3301	*nqrE*	NADH:ubiquinone oxidoreductase, subunit E	YPIII_E25	**2,0**	2,0E-02
YPK_3320	*mtnC*	2,3-diketo-5-methylthio-1-phosphopentane phosphatase	YPIII_E25	**4,2**	1,5E-04
YPK_3885	*hemN*	coproporphyrinogen dehydrogenase	YPIII_E25	**8,8**	1,2E-04
YPK_3992	*glpQ*	glycerophosphoryl diester phosphodiesterase	YPIII_E25	**8,1**	1,6E-05
YPK_4113	*glpK*	glycerol kinase	YPIII_E25	**5,0**	2,4E-15
YPK_4219	*atpI*	ATP synthase I chain	YPIII_E25	**3,1**	7,9E-04
YPK_4220	*atpB*	ATP synthase F0, A subunit	YPIII_E25	**2,7**	1,9E-06

Locus	Gene name	Gene description	Condition upregulated	Fold change	p-vale
YPK_4221	*atpE*	ATP synthase F0, C subunit	YPIII_E25	**2,3**	3,6E-05
YPK_4223	*atpH*	ATP synthase F1, delta subunit	YPIII_E25	**2,1**	3,1E-04
YPK_4225	*atpG*	ATP synthase F1, gamma subunit	YPIII_E25	**2,2**	9,7E-05
YPK_4226	*atpD*	ATP synthase F1, beta subunit	YPIII_E25	**2,2**	8,7E-05
YPK_4227	*atpC*	ATP synthase F1, epsilon subunit	YPIII_E25	**2,7**	2,2E-02
YPK_0036	*fdhD*	formate dehydrogenase family accessory protein FdhD	YPIII_E37	**2,3**	2,8E-02
YPK_0037	*fdoG-1*	molybdopterin oxidoreductase Fe4S4 region	YPIII_E37	**2,0**	3,0E-04
YPK_0038	*fdoG-2*	formate dehydrogenase, alpha subunit	YPIII_E37	**2,7**	2,9E-07
YPK_0039	*fdoH*	formate dehydrogenase, beta subunit	YPIII_E37	**2,5**	4,7E-06
YPK_0098	*dctA*	sodium:dicarboxylate symporter	YPIII_E37	**2,4**	2,6E-03
YPK_0174	*pckA*	phosphoenolpyruvate carboxykinase (ATP)	YPIII_E37	**5,2**	4,9E-15
YPK_0364	*aceB*	malate synthase A	YPIII_E37	**4,5**	2,9E-02
YPK_0365	*aceA*	isocitrate lyase	YPIII_E37	**5,2**	3,4E-04
YPK_0461	*yedZ*	ferric reductase domain protein transmembrane component domain	YPIII_E37	**5,4**	4,5E-08
YPK_0563	*fadH*	NADH:flavin oxidoreductase/NADH oxidase	YPIII_E37	**4,4**	1,0E-09
YPK_0600		Na+/H+ antiporter NhaC	YPIII_E37	**5,3**	6,7E-11
YPK_0668	*yqhD*	iron-containing alcohol dehydrogenase	YPIII_E37	**2,5**	7,5E-04
YPK_1061		flavodoxin/nitric oxide synthase	YPIII_E37	**2,2**	1,3E-02
YPK_1391	*maeB*	malate dehydrogenase (oxaloacetate-decarboxylating) (NADP(+)), Phosphate acetyltransferase	YPIII_E37	**4,4**	4,0E-10
YPK_1441		aldo/keto reductase	YPIII_E37	**2,1**	1,2E-02
YPK_1845	*ydiJ; yhaK; yhhW*	FAD linked oxidase domain protein	YPIII_E37	**2,6**	1,6E-05
YPK_1871	*nemA*	N-ethylmaleimide reductase	YPIII_E37	**2,7**	3,3E-05
YPK_1974	*aldA*	aldehyde Dehydrogenase_	YPIII_E37	**22,3**	1,3E-22
YPK_2227	*astD*	succinylglutamic semialdehyde dehydrogenase	YPIII_E37	**4,3**	5,6E-03
YPK_2268		acetyl-CoA hydrolase/transferase	YPIII_E37	**3,5**	9,8E-03
YPK_2369	*putA*	delta-1-pyrroline-5-carboxylate dehydrogenase	YPIII_E37	**2,3**	2,6E-05
YPK_2459	*hpaE*	5-carboxymethyl-2-hydroxymuconate semialdehyde dehydrogenase	YPIII_E37	**10,2**	3,9E-02
YPK_2506	*lldD*	FMN-dependent alpha-hydroxy acid dehydrogenase	YPIII_E37	**8,1**	6,1E-17
YPK_2770	*xylB*	xylulokinase	YPIII_E37	**2,6**	1,8E-02
YPK_2771	*gabD-2*	aldehyde dehydrogenase	YPIII_E37	**3,1**	8,5E-03
YPK_2966	*sucC*	succinyl-CoA synthetase, beta subunit	YPIII_E37	**2,2**	1,0E-05
YPK_2967	*sucB*	2-oxoglutarate dehydrogenase, E2 subunit, dihydrolipoamide succinyltransferase	YPIII_E37	**2,4**	1,6E-06
YPK_2968	*kgd*	2-oxoglutarate dehydrogenase, E1 subunit	YPIII_E37	**2,3**	1,8E-05
YPK_2969	*sdhB*	succinate dehydrogenase and fumarate reductase iron-sulfur protein	YPIII_E37	**2,5**	5,6E-06
YPK_2970	*sdhA*	succinate dehydrogenase, flavoprotein subunit	YPIII_E37	**2,4**	2,9E-06
YPK_2973	*gltA*	citrate synthase I	YPIII_E37	**2,7**	1,7E-06
YPK_3004	*ubiF*	ubiquinone biosynthesis hydroxylase, UbiH/UbiF/VisC/COQ6 family	YPIII_E37	**2,4**	1,7E-03
YPK_3005	*miaB*	tRNA-i(6)A37 thiotransferase enzyme MiaB	YPIII_E37	**2,1**	4,7E-04
YPK_3381	*glpK*	glycerol kinase	YPIII_E37	**2,4**	2,8E-02
YPK_3389	cybC-2	cytochrome b562	YPIII_E37	**23,6**	8,8E-07
YPK_3390	*cybB*	cytochrome B561	YPIII_E37	**18,6**	4,5E-21
YPK_3403	*sgbK*	carbohydrate kinase FGGY	YPIII_E37	**3,5**	4,1E-02
YPK_3404	*fumA*	hydro-lyase, Fe-S type, tartrate/fumarate subfamily, beta subunit	YPIII_E37	**3,8**	6,0E-11
YPK_3648	*ydeV*	carbohydrate kinase FGGY	YPIII_E37	**6,9**	4,0E-05
YPK_3813	*frdA*	fumarate reductase, flavoprotein subunit	YPIII_E37	**5,5**	7,1E-12
YPK_3814	*frdB*	succinate dehydrogenase and fumarate reductase iron-sulfur protein	YPIII_E37	**4,6**	9,6E-09
YPK_3815	*frdC*	fumarate reductase subunit C	YPIII_E37	**4,0**	7,7E-03
YPK_3816	*frdD*	fumarate reductase D subunit	YPIII_E37	**3,4**	5,4E-03
YPK_3829	*fdhF*	formate dehydrogenase, alpha subunit	YPIII_E37	**2,1**	3,9E-02
YPK_3989	*glpC*	glycerol-3-phosphate dehydrogenase, anaerobic, C subunit	YPIII_E37	**2,3**	1,0E-02
YPK_4078	*sthA*	pyridine nucleotide-disulphide oxidoreductase dimerisation region	YPIII_E37	**2,9**	2,3E-07
Carbohydrate transport and metabolism					
YPK_0376	*malG*	binding-protein-dependent transport systems inner membrane component	YPIII_E25	**5,1**	6,5E-03
YPK_0381	*lamB-1*	porin LamB type	YPIII_E25	**6,6**	4,4E-02
YPK_1273	*suhB*	inositol-phosphate phosphatase	YPIII_E25	**4,8**	6,1E-11
YPK_1834	*pmrJ*	polysaccharide deacetylase	YPIII_E25	**2,5**	2,2E-02
YPK_1855	*pykF*	pyruvate kinase	YPIII_E25	**2,7**	5,2E-07
YPK_1948	*yrfG-2, yigB-2, yihX-2*	HAD-superfamily hydrolase, subfamily IA, variant 1	YPIII_E25	**2,6**	3,4E-03
YPK_3321	*mtnB*	methylthioribulose-1-phosphate dehydratase	YPIII_E25	**3,0**	4,0E-02
YPK_3491	*aceE*	2-oxo-acid dehydrogenase E1 subunit, homodimeric type	YPIII_E25	**2,0**	3,4E-04
YPK_3887		NmrA family protein	YPIII_E25	**5,4**	6,1E-06
YPK_4112	*glpF*	MIP family channel protein	YPIII_E25	**8,1**	2,8E-22
YPK_0026	*mtlA*	PTS system, mannitol-specific IIC subunit	YPIII_E37	**3,0**	4,6E-04
YPK_0027	*mtlD*	mannitol dehydrogenase domain	YPIII_E37	**2,9**	9,2E-04
YPK_0147	*glgB*	1,4-alpha-glucan branching enzyme	YPIII_E37	**2,1**	6,0E-04
YPK_0148	*glgX*	glycogen debranching enzyme GlgX	YPIII_E37	**2,9**	1,8E-04
YPK_0150	*glgA*	glycogen/starch synthase, ADP-glucose type	YPIII_E37	**4,2**	2,5E-07
YPK_0151	*glgP-1*	glycogen/starch/alpha-glucan phosphorylase	YPIII_E37	**9,3**	9,2E-25
YPK_0241	*celF*	glycoside hydrolase family 4	YPIII_E37	**6,2**	1,0E-10
YPK_0431	*yphF-1, ytfQ-1*	carbohydrate uptake (CUT2 family) ABC transporter, periplasmic carbohydrate-binding protein	YPIII_E37	**9,1**	7,8E-18
YPK_0435		FGGY-family pentulose kinase	YPIII_E37	**2,9**	4,8E-04
YPK_0494	*treC*	alpha,alpha-phosphotrehalase	YPIII_E37	**3,0**	2,6E-06
YPK_0495	*treB*	PTS system, trehalose-specific IIBC subunit	YPIII_E37	**3,2**	3,4E-07
YPK_0501	*ptsO*	Phosphotransferase system, phosphocarrier protein HPr	YPIII_E37	**2,1**	2,0E-02
YPK_0554	*uxaC*	glucuronate isomerase	YPIII_E37	**5,2**	1,1E-07
YPK_0555	*uxaB*	mannitol dehydrogenase domain	YPIII_E37	**5,3**	2,7E-05
YPK_0556	*uxaA*	altronate dehydratase	YPIII_E37	**2,5**	6,5E-03
YPK_0812	*rbsB-1*	ribose transport system substrate-binding protein	YPIII_E37	**3,4**	1,7E-03
YPK_0814	*rbsC*	monosaccharide-transporting ATPase	YPIII_E37	**6,0**	1,2E-04
YPK_0964	*xltC*	periplasmic binding protein/LacI transcriptional regulator	YPIII_E37	**13,1**	2,9E-09
YPK_0971	*ganQ*	binding-protein-dependent transport systems inner membrane component	YPIII_E37	**2,7**	7,3E-03
YPK_0972		arabinogalactan endo-1,4-beta-galactosidase	YPIII_E37	**2,6**	1,2E-03
YPK_0973	*bgaB*	beta-galactosidase	YPIII_E37	**3,1**	1,9E-05
YPK_0975	*lamB-2*	porin LamB type	YPIII_E37	**2,4**	7,3E-03
YPK_0990	*agaE*	PTS system mannose/fructose/sorbose family IID component	YPIII_E37	**2,5**	4,8E-02
YPK_1111	*hpxB*	urate catabolism protein	YPIII_E37	**2,4**	2,5E-03
YPK_1144	*celA*	phosphotransferase system lactose/cellobiose-specific IIB subunit	YPIII_E37	**9,3**	3,5E-02
YPK_1540	*hisM*	polar amino acid ABC transporter, inner membrane subunit	YPIII_E37	**4,5**	2,4E-02
YPK_1546	*ulaA*	putative sugar-specific permease SgaT/UlaA	YPIII_E37	**3,5**	8,5E-09
YPK_1547	*ulaB*	phosphotransferase system lactose/cellobiose-specific IIB subunit	YPIII_E37	**3,1**	3,4E-07

Locus	Gene name	Gene description	Condition upregulated	Fold change	p-vale
YPK_1548	*ulaC*	putative PTS IIA-like nitrogen-regulatory protein PtsN	YPIII_E37	**2,7**	3,5E-06
YPK_1611	*rbsB-2*	monosaccharide-transporting ATPase	YPIII_E37	**128,3**	3,6E-11
YPK_1694	*ptsG*	PTS system, glucose-specific IIBC subunit	YPIII_E37	**4,4**	4,5E-13
YPK_1727		NmrA family protein	YPIII_E37	**2,6**	1,1E-02
YPK_1739	*lacZ*	glycoside hydrolase family 2 TIM barrel	YPIII_E37	**2,3**	4,0E-03
YPK_1798	*togB*	extracellular solute-binding protein family 1	YPIII_E37	**3,5**	2,7E-02
YPK_1804	*kduI*	4-deoxy-L-threo-5-hexosulose-uronate ketol-isomerase	YPIII_E37	**2,9**	2,7E-02
YPK_1811	*yniA*	fructosamine kinase	YPIII_E37	**2,5**	4,2E-03
YPK_1999	*araF*	monosaccharide-transporting ATPase	YPIII_E37	**4,2**	1,8E-02
YPK_2014		NAD-dependent epimerase/dehydratase	YPIII_E37	**5,7**	3,3E-02
YPK_2019	*mipB*	transaldolase	YPIII_E37	**2,3**	3,1E-02
YPK_2266	*citE*	putative citrate lyase beta chain	YPIII_E37	**4,1**	1,7E-02
YPK_2566	*mglB*	periplasmic binding protein/LacI transcriptional regulator	YPIII_E37	**3,2**	8,2E-08
YPK_2706		NAD-dependent epimerase/dehydratase	YPIII_E37	**4,9**	1,6E-08
YPK_2768	*yphF-4, ytfQ-4*	ABC transporter, periplasmic sugar-binding protein	YPIII_E37	**5,7**	2,6E-02
YPK_2769	*rpiA*	ribose 5-phosphate isomerase	YPIII_E37	**8,1**	5,4E-04
YPK_2778	*uxuA*	mannonate dehydratase	YPIII_E37	**2,6**	7,5E-05
YPK_2779	*uxuB*	mannitol dehydrogenase domain	YPIII_E37	**4,8**	6,5E-05
YPK_2825		class II aldolase/adducin family protein	YPIII_E37	**4,0**	3,0E-04
YPK_2996	*nagE*	PTS system, N-acetylglucosamine-specific IIBC subunit	YPIII_E37	**2,5**	6,5E-06
YPK_2997	*nagB*	glucosamine-6-phosphate isomerase	YPIII_E37	**3,1**	9,9E-07
YPK_2998	*nagA*	N-acetylglucosamine-6-phosphate deacetylase	YPIII_E37	**2,9**	3,5E-06
YPK_3380		L-fucose isomerase-like protein	YPIII_E37	**3,3**	1,4E-02
YPK_3398	*yphF-5, ytfQ-5*	carbohydrate uptake ABC transporter 2 (CUT2) family, periplasmic carbohydrate-binding protein	YPIII_E37	**12,1**	4,9E-03
YPK_3419	*dhaK*	glycerone kinase	YPIII_E37	**4,2**	3,2E-03
YPK_3639	*ybhC*	pectinesterase	YPIII_E37	**7,0**	1,3E-08
YPK_3654	*yneB*	deoxyribose-phosphate aldolase/phospho-2-dehydro-3-deoxyheptonate aldolase	YPIII_E37	**16,9**	4,0E-08
YPK_3707	*ycjP-2*	binding-protein-dependent transport systems inner membrane component	YPIII_E37	**4,1**	1,8E-02
YPK_3709	*ycjN*	extracellular solute-binding protein family 1	YPIII_E37	**7,3**	2,3E-04
YPK_4210	*rbsD*	RbsD or FucU transport	YPIII_E37	**3,3**	2,1E-07
Amino acid transport and metabolism					
YPK_0005	*ybhA, ybjI, yidA, yigL*	sugar phosphatase	YPIII_E25	**3,0**	5,1E-04
YPK_0225	*aroK*	shikimate kinase	YPIII_E25	**2,2**	3,8E-04
YPK_0238	*tsgA*	major facilitator superfamily MFS_1	YPIII_E25	**7,3**	2,1E-06
YPK_0785	*iucB*	putative siderophore biosynthesis protein IucB	YPIII_E25		5,6E-04
YPK_0788		major facilitator superfamily MFS_1	YPIII_E25	**6,4**	1,7E-03
YPK_0811	*speC*	ornithine decarboxylase	YPIII_E25	**2,5**	4,0E-03
YPK_0845	*speA*	arginine decarboxylase	YPIII_E25	**2,1**	3,7E-04
YPK_1096	*metN-1*	D-methionine ABC transporter, ATPase subunit	YPIII_E25	**2,6**	3,5E-05
YPK_1462	*sfuB*	binding-protein-dependent transport systems inner membrane component	YPIII_E25	**3,0**	6,4E-04
YPK_1939	*arcD, lys1, lysP*	arginine/ornithine antiporter	YPIII_E25	**2,2**	7,7E-03
YPK_2041	*trpH*	PHP domain protein	YPIII_E25	**2,2**	1,7E-02
YPK_2106	*bcr*	drug resistance transporter, Bcr/CflA subfamily	YPIII_E25	**4,3**	3,8E-05
YPK_2256	*ansP*	amino acid permease-associated region	YPIII_E25	**2,7**	3,9E-04
YPK_2487	*mdlA-2*	ABC transporter related	YPIII_E25	**2,7**	3,9E-04
YPK_2517	*yeeF*	amino acid permease-associated region	YPIII_E25	**10,1**	9,5E-26
YPK_2526	*hisD*	histidinol dehydrogenase	YPIII_E25	**3,5**	1,9E-03
YPK_2581	*ybiT*	ABC transporter related	YPIII_E25	**2,8**	1,3E-06
YPK_2711	*artI*	cationic amino acid ABC transporter, periplasmic binding protein	YPIII_E25	**2,1**	1,1E-02
YPK_2712	*artQ*	polar amino acid ABC transporter, inner membrane subunit	YPIII_E25	**3,4**	3,8E-02
YPK_2752	*lysP*	amino acid permease-associated region	YPIII_E25	**3,2**	2,9E-06
YPK_2776	*mtr*	aromatic amino acid transporter	YPIII_E25	**8,9**	6,4E-03
YPK_2858	*yedA*	putative inner membrane transporter YedA	YPIII_E25	**3,6**	2,5E-02
YPK_2942		abortive infection protein	YPIII_E25	**5,7**	4,4E-04
YPK_3272	*proY*	amino acid permease-associated region	YPIII_E25	**2,3**	1,6E-03
YPK_3273	*brnQ*	branched-chain amino acid transport system II carrier protein	YPIII_E25	**2,8**	1,5E-03
YPK_3317	*mtnK*	5-methylthioribose kinase	YPIII_E25	**5,3**	1,1E-03
YPK_3322	*ybdL*	aminotransferase class I and II	YPIII_E25	**3,8**	1,3E-03
YPK_3477	*yadG*	ABC transporter related	YPIII_E25	**2,4**	1,5E-04
YPK_3595	*yaaH*	GPR1/FUN34/yaaH family protein	YPIII_E25	**24,0**	9,9E-15
YPK_3755		DMT family amino acid efflux protein	YPIII_E25	**4,0**	5,8E-04
YPK_3893	*hmuV*	ABC transporter related	YPIII_E25	**3,7**	2,8E-03
YPK_3952	*metE*	5-methyltetrahydropteroyltriglutamate--homocysteine S-methyltransferase	YPIII_E25	**3,3**	1,2E-03
YPK_3991	*glpA*	glycerol-3-phosphate dehydrogenase, anaerobic, A subunit	YPIII_E25	**4,7**	1,3E-04
YPK_4021	*mmuP, yifK*	amino acid permease-associated region	YPIII_E25	**3,6**	7,3E-06
YPK_4060	*ilvM*	acetolactate synthase isozyme II small subunit	YPIII_E25	**2,7**	3,0E-02
YPK_4189	*glnA*	glutamine synthetase, type I	YPIII_E25	**3,6**	4,9E-10
pYV0007	*repB, copB*	repB, repA2, copB; putative replication transcriptional regulator	YPIII_E37	**2,3**	2,9E-02
YPK_0017	*ghrB*	D-isomer specific 2-hydroxyacid dehydrogenase NAD-binding	YPIII_E37	**2,2**	4,1E-02
YPK_0076	*hutU*	urocanate hydratase	YPIII_E37	**2,7**	4,9E-02
YPK_0432	*yphE-1; ytfR-1*	ABC transporter related	YPIII_E37	**2,1**	1,5E-02
YPK_0599		aminotransferase class I and II	YPIII_E37	**6,2**	9,9E-15
YPK_0762	*gntP*	gluconate transporter	YPIII_E37	**4,6**	3,4E-03
YPK_0813	*rbsA-1*	ABC transporter related	YPIII_E37	**3,7**	7,8E-03
YPK_0867	*gcvT*	glycine cleavage system T protein	YPIII_E37	**6,4**	1,3E-17
YPK_0868	*gcsH*	glycine cleavage system H protein	YPIII_E37	**5,0**	3,7E-11
YPK_0869	*gcvP*	glycine dehydrogenase	YPIII_E37	**6,1**	1,1E-17
YPK_0965	*xltB*	monosaccharide-transporting ATPase	YPIII_E37	**15,6**	4,8E-06
YPK_0966	*xltA*	ABC transporter related	YPIII_E37	**47,6**	7,2E-17
YPK_1063	*dapD*	2,3,4,5-tetrahydropyridine-2,6-dicarboxylate N-succinyltransferase	YPIII_E37	**2,7**	1,2E-07
YPK_1131	*ureA*	urease, gamma subunit	YPIII_E37	**9,9**	1,2E-10
YPK_1132	*ureB*	urease, beta subunit	YPIII_E37	**11,5**	1,8E-08
YPK_1133	*ureC*	urease, alpha subunit	YPIII_E37	**11,8**	3,5E-12
YPK_1136	*ureG*	urease accessory protein UreG	YPIII_E37	**5,7**	2,0E-07
YPK_1138	*utp*	urea transporter	YPIII_E37	**2,5**	1,9E-02
YPK_1349	*speG*	GCN5-related N-acetyltransferase	YPIII_E37	**2,6**	2,6E-05
YPK_1407	*nanT*	major facilitator superfamily MFS_1	YPIII_E37	**2,3**	9,4E-04
YPK_1429	*cysK*	cysteine synthase A	YPIII_E37	**5,6**	3,5E-05
YPK_1538	*hisJ*	cationic amino acid ABC transporter, periplasmic binding protein	YPIII_E37	**4,4**	2,1E-10
YPK_1539	*hisQ*	polar amino acid ABC transporter, inner membrane subunit	YPIII_E37	**9,2**	3,0E-05
YPK_1541	*hisP*	ABC transporter related	YPIII_E37	**3,8**	2,7E-03
YPK_1594	*ybiB*	glycosyl transferase family 3	YPIII_E37	**3,2**	4,7E-04

Locus	Gene name	Gene description	Condition upregulated	Fold change	p-vale
YPK_1610	*gutB*	alcohol dehydrogenase zinc-binding domain protein	YPIII_E37	**60,1**	1,8E-15
YPK_1612	*rbsA-2*	ABC transporter related	YPIII_E37		9,9E-04
YPK_1906	*mppA*	extracellular solute-binding protein family 5	YPIII_E37	**2,1**	1,9E-03
YPK_1983	*ynfM*	major facilitator superfamily MFS_1	YPIII_E37	**4,4**	7,5E-03
YPK_1998	*araG*	ABC transporter related	YPIII_E37	**9,6**	9,5E-04
YPK_2030	*acnA*	aconitate hydratase 1	YPIII_E37	**6,3**	5,6E-10
YPK_2107	*dadA*	D-amino-acid dehydrogenase	YPIII_E37	**3,1**	6,2E-07
YPK_2223	*hutG*	N-formylglutamate amidohydrolase	YPIII_E37	**2,3**	1,7E-02
YPK_2226	*astB*	succinylarginine dihydrolase	YPIII_E37	**3,5**	3,1E-02
YPK_2228	*astA*	arginine N-succinyltransferase	YPIII_E37	**5,7**	1,9E-02
YPK_2229	*astC*	succinylornithine transaminase family	YPIII_E37	**7,7**	2,4E-05
YPK_2376	*fliY*	extracellular solute-binding protein family 3	YPIII_E37	**2,0**	1,8E-02
YPK_2409	*yphE-2; ytfR-2*	ABC transporter related	YPIII_E37	**5,1**	1,0E-02
YPK_2452	*hpaC*	4-hydroxyphenylacetate 3-monooxygenase, reductase subunit	YPIII_E37	**6,1**	1,8E-03
YPK_2503		major facilitator superfamily MFS_1	YPIII_E37	**16,2**	1,6E-02
YPK_2564	*mglC*	monosaccharide-transporting ATPase	YPIII_E37	**3,7**	2,6E-08
YPK_2565	*mglA*	ABC transporter related	YPIII_E37	**3,4**	3,0E-05
YPK_2674	*ansB*	L-asparaginase, type II	YPIII_E37	**28,2**	3,5E-08
YPK_2703	*poxB*	thiamine pyrophosphate protein TPP binding domain protein	YPIII_E37	**5,4**	1,0E-11
YPK_2705	*ltaA*	threonine aldolase	YPIII_E37	**3,2**	2,5E-05
YPK_2709	*pheA-1*	chorismate mutase	YPIII_E37	**2,4**	2,3E-04
YPK_2786	*yejA*	extracellular solute-binding protein family 5	YPIII_E37	**4,2**	5,2E-11
YPK_2787	*yejB*	binding-protein-dependent transport systems inner membrane component	YPIII_E37	**4,4**	4,7E-08
YPK_2788	*yejE*	binding-protein-dependent transport systems inner membrane component	YPIII_E37	**3,5**	1,8E-05
YPK_2789	*yejF*	ABC transporter related	YPIII_E37	**4,2**	2,2E-08
YPK_2901	*yadG, ybhF*	ABC transporter related	YPIII_E37	**2,5**	2,1E-02
YPK_3010	*ybeJ/gltI*	extracellular solute-binding protein family 3	YPIII_E37	**3,7**	2,6E-09
YPK_3269	*ggt*	gamma-glutamyltransferase	YPIII_E37	**2,9**	1,1E-02
YPK_3325	*pucG*	aminotransferase class V	YPIII_E37	**3,8**	4,1E-03
YPK_3399	*yphE-5; ytfR-5*	ABC transporter related	YPIII_E37	**13,7**	2,3E-02
YPK_3421	*ydjJ*	alcohol dehydrogenase zinc-binding domain protein	YPIII_E37	**9,5**	9,3E-08
YPK_3436	*cysD*	sulfate adenylyltransferase, small subunit	YPIII_E37	**6,6**	8,6E-09
YPK_3440	*cysH*	phosphoadenosine phosphosulfate reductase	YPIII_E37	**4,3**	2,4E-10
YPK_3487	*acnB*	aconitate hydratase 2	YPIII_E37	**2,5**	1,8E-06
YPK_3650	*ego*	ABC transporter related	YPIII_E37		1,5E-06
YPK_3706	*msmX, msmK, malK, sugC, ggtA, msiK*	ABC transporter related	YPIII_E37	**2,2**	1,4E-02
YPK_3825	*aspA*	aspartate ammonia-lyase	YPIII_E37	**3,0**	3,1E-08
YPK_3923	*actP*	cation/acetate symporter ActP	YPIII_E37	**16,3**	2,5E-24
YPK_4088	*argB*	acetylglutamate kinase	YPIII_E37	**2,3**	1,5E-02
YPK_4237		extracellular solute-binding protein family 3	YPIII_E37	**2,8**	1,1E-03
Nucleotide transport and metabolism					
YPK_1251	*tadA*	tRNA-specific adenosine deaminase	YPIII_E25	**2,0**	2,5E-02
YPK_1352	*upp*	uracil phosphoribosyltransferase	YPIII_E25	**2,9**	2,9E-03
YPK_1353	*pyrP, uraA*	uracil-xanthine permease	YPIII_E25	**3,1**	4,6E-03
YPK_1438	*nupC1*	nucleoside transporter	YPIII_E25	**2,4**	1,9E-05
YPK_2669	*cmk*	cytidylate kinase	YPIII_E25	**2,1**	2,9E-04
YPK_2737	*deoC-1*	deoxyribose-phosphate aldolase	YPIII_E25	**3,0**	2,7E-02
YPK_3291	*gpt*	xanthine phosphoribosyltransferase	YPIII_E25	**2,2**	1,2E-03
YPK_3624	*deoD*	purine nucleoside phosphorylase	YPIII_E25	**2,0**	4,8E-04
YPK_3626	*deoA*	thymidine phosphorylase	YPIII_E25	**2,6**	9,1E-04
YPK_3627	*deoC-2*	deoxyribose-phosphate aldolase	YPIII_E25	**2,4**	1,0E-02
YPK_3793	*purA*	adenylosuccinate synthase	YPIII_E25	**2,3**	3,6E-05
YPK_0499	*pyrI*	aspartate carbamoyltransferase, regulatory subunit	YPIII_E37	**2,1**	4,4E-02
YPK_0500	*pyrB*	aspartate carbamoyltransferase	YPIII_E37	**3,0**	4,0E-03
YPK_1117	*nrdE*	ribonucleoside-diphosphate reductase, alpha subunit	YPIII_E37	**2,4**	1,6E-02
YPK_2220	*hutF*	formiminoglutamate deiminase	YPIII_E37	**2,6**	2,3E-02
YPK_3691	*nrdD*	anaerobic ribonucleoside-triphosphate reductase	YPIII_E37	**5,2**	1,3E-04
Coenzyme transport and metabolism					
YPK_0649	*ribB*	3,4-dihydroxy-2-butanone 4-phosphate synthase	YPIII_E25	**2,0**	3,5E-03
YPK_0843	*metK*	methionine adenosyltransferase	YPIII_E25	**4,1**	4,6E-08
YPK_3250	*thiI*	thiamine biosynthesis/tRNA modification protein ThiI	YPIII_E25	**4,8**	1,7E-10
YPK_3255	*thiL*	thiamine-monophosphate kinase	YPIII_E25	**2,2**	1,1E-03
YPK_3443	*ygcM*	queuosine biosynthesis protein QueD	YPIII_E25	**3,8**	8,9E-06
YPK_3542	*tbpA*	thiamine ABC transporter, periplasmic binding protein	YPIII_E25	**2,4**	1,7E-02
YPK_4200	*mobB*	molybdopterin-guanine dinucleotide biosynthesis protein B	YPIII_E25	**3,2**	2,1E-02
YPK_0860	*ygfA*	5-formyltetrahydrofolate cyclo-ligase	YPIII_E37	**2,4**	1,1E-03
YPK_2214		adenylate-forming enzyme	YPIII_E37	**3,3**	3,3E-02
YPK_3437	*cysG*	uroporphyrin-III C-methyltransferase	YPIII_E37	**5,3**	1,8E-06
YPK_3763	*yhcN*	protein of unknown function DUF1471	YPIII_E37	**4,9**	5,6E-04
YPK_4209		ribokinase	YPIII_E37	**3,7**	6,3E-04
Lipid transport and metabolism					
YPK_1520	*fabB*	beta-ketoacyl synthase	YPIII_E25	**2,8**	4,0E-07
YPK_1683	*plsX*	fatty acid/phospholipid synthesis protein PlsX	YPIII_E25	**2,2**	3,4E-04
YPK_1688	*fabF*	3-oxoacyl-(acyl-carrier-protein) synthase 2	YPIII_E25	**4,5**	3,3E-12
YPK_2634	*fabA*	beta-hydroxyacyl-(acyl-carrier-protein) dehydratase FabA	YPIII_E25	**2,3**	1,2E-04
YPK_0105	*cdh*	CDP-diacylglycerol diphosphatase	YPIII_E37	**4,0**	3,8E-05
YPK_0447		3-hydroxyisobutyrate dehydrogenase	YPIII_E37	**7,6**	1,4E-02
YPK_1508	*fadI*	acetyl-CoA C-acyltransferase FadI	YPIII_E37	**7,7**	6,9E-16
YPK_1509	*fadJ*	fatty acid oxidation complex, alpha subunit FadJ	YPIII_E37	**8,1**	4,9E-17
YPK_1803	*kduD1*	2-deoxy-D-gluconate 3-dehydrogenase	YPIII_E37	**2,4**	1,1E-02
YPK_1924	*acpD*	NAD(P)H dehydrogenase (quinone)	YPIII_E37	**2,2**	3,6E-03
YPK_2125	*fadD-1*	AMP-dependent synthetase and ligase	YPIII_E37	**7,3**	2,6E-16
YPK_2413		short-chain dehydrogenase/reductase SDR	YPIII_E37	**4,8**	3,1E-04
YPK_2636	*fabF2*	3-oxoacyl-(acyl-carrier-protein) synthase 2	YPIII_E37	**2,1**	4,2E-03
YPK_3309	*fadE*	acyl-CoA dehydrogenase	YPIII_E37	**12,6**	6,3E-14
YPK_3420		short-chain dehydrogenase/reductase SDR	YPIII_E37	**5,8**	4,9E-05
YPK_3532	*fadD-2*	AMP-dependent synthetase and ligase	YPIII_E37	**3,8**	2,4E-06
YPK_3714		sterol-binding domain protein	YPIII_E37	**2,4**	2,8E-05
YPK_3788	*aidB*	acyl-CoA dehydrogenase domain protein	YPIII_E37	**2,6**	3,1E-04

Locus	Gene name	Gene description	Condition upregulated	Fold change	p-vale
YPK_3933	*fadB*	fatty oxidation complex, alpha subunit FadB	YPIII_E37	**15,7**	1,9E-24
YPK_3934	*fadA*	acetyl-CoA C-acyltransferase FadA	YPIII_E37	**17,1**	1,0E-29
Secondary metabolites biosynthesis, transport and catabolism					
YPK_0783	*iucD*	L-lysine 6-monooxygenase (NADPH)	YPIII_E25	**11,3**	4,5E-10
YPK_0784	*iucC*	IucA/IucC family protein	YPIII_E25	**18,4**	2,1E-03
YPK_0786	*rhbC*	IucA/IucC family protein	YPIII_E25	**31,5**	2,0E-05
YPK_0821	*trmB*	tRNA (guanine-N(7)-)-methyltransferase	YPIII_E25	**2,1**	2,6E-03
YPK_2538		IucA/IucC family siderophore biosynthesis protein	YPIII_E25	**3,1**	3,3E-02
YPK_4218	*gidB*	methyltransferase GidB	YPIII_E25	**2,1**	3,4E-03
YPK_0751		amino acid adenylation domain protein	YPIII_E37	**2,7**	2,2E-02
YPK_0752		amino acid adenylation domain protein	YPIII_E37	**2,4**	4,5E-03
YPK_0825		virulence determinant	YPIII_E37	**3,5**	7,3E-04
YPK_1593	*menE*	O-succinylbenzoate-CoA ligase	YPIII_E37	**2,5**	1,4E-03
YPK_1858	*cfa*	cyclopropane-fatty-acyl-phospholipid synthase	YPIII_E37	**2,8**	3,2E-04
YPK_2203		methyltransferase type 12	YPIII_E37	**20,9**	3,6E-10
YPK_2222	*hutI*	imidazolonepropionase	YPIII_E37	**2,4**	4,2E-02
YPK_2453	*hpaB*	4-hydroxyphenylacetate 3-monooxygenase, oxygenase subunit	YPIII_E37	**7,1**	1,3E-02
YPK_3921	*rcs*	acetate-CoA ligase	YPIII_E37	**30,3**	1,0E-29
Inorganic ion transport and metabolism					
YPK_0068	*fhuC-1, fepC-1, fecE-1*	ABC transporter related	YPIII_E25	**2,9**	4,4E-02
YPK_0069	*fhuB-1, fepG-1, fecD-1*	transport system permease protein	YPIII_E25	**4,4**	1,1E-02
YPK_0070	*fhuB-2, fepG-2, fecD-2*	transport system permease protein	YPIII_E25	**8,6**	1,3E-04
YPK_0071	*fhuD-1, fepB-1, fecB-1*	periplasmic binding protein	YPIII_E25	**8,7**	9,6E-13
YPK_0122	*pitA*	phosphate transporter	YPIII_E25	**3,8**	7,4E-12
YPK_0782	*iutA*	TonB-dependent siderophore receptor	YPIII_E25	**7,7**	4,1E-12
YPK_0815	*fhuA, yncD*	TonB-dependent siderophore receptor	YPIII_E25	**10,6**	9,4E-16
YPK_0816	*fhuD-2, fepB-2, fecB-2*	periplasmic binding protein	YPIII_E25	**18,7**	1,5E-07
YPK_1094	*metQ-1*	lipoprotein, YaeC family	YPIII_E25	**2,6**	2,8E-04
YPK_1095	*metI*	DL-methionine transporter permease	YPIII_E25	**2,2**	7,6E-03
YPK_1463	*sfuA*	extracellular solute-binding protein family 1	YPIII_E25	**6,7**	3,7E-10
YPK_1658	*cvrA, nhaP2*	sodium/hydrogen exchanger	YPIII_E25	**2,5**	5,2E-05
YPK_2110	*nhaB*	Na+/H+ antiporter NhaB	YPIII_E25	**2,8**	3,4E-03
YPK_2251		periplasmic protein-probably involved in high-affinity Fe2+ transport	YPIII_E25	**3,2**	3,0E-03
YPK_2252	*efeU-1*	iron permease FTR1	YPIII_E25	**2,5**	5,9E-03
YPK_2365	*efeO*	iron uptake system component EfeO	YPIII_E25	**2,6**	4,2E-05
YPK_2366	*efeU-2*	high-affinity iron transporter	YPIII_E25	**3,1**	5,7E-05
YPK_2469	*fcuA*	TonB-dependent siderophore receptor	YPIII_E25	**36,1**	2,2E-34
YPK_2548	*fhuF*	ferric iron reductase	YPIII_E25		3,3E-03
YPK_2748	*fepA-1, cirA-1*	TonB-dependent receptor	YPIII_E25	**14,1**	5,5E-17
YPK_2749	*fhuC-2, fepC-2, fecE-2*	ABC transporter related	YPIII_E25	**4,4**	8,8E-05
YPK_2750	*fhuB-3, fepG-3, fecD-3*	transport system permease protein	YPIII_E25	**7,1**	2,7E-07
YPK_2751	*fhuD-3, fepB-3, fecB-3*	periplasmic binding protein	YPIII_E25	**27,6**	9,4E-26
YPK_3409	*fepA-2, cirA-2*	TonB-dependent receptor	YPIII_E25	**7,1**	3,2E-06
YPK_3460	*fhuB*	transport system permease protein	YPIII_E25	**3,5**	1,9E-04
YPK_3461	*fhuD*	periplasmic binding protein	YPIII_E25	**6,1**	4,3E-06
YPK_3462	*fhuC*	ABC transporter related	YPIII_E25	**3,9**	1,5E-04
YPK_3886	*chuX*	putative heme iron utilization protein	YPIII_E25	**3,8**	4,8E-04
YPK_3888	*hemP*	hemin uptake protein	YPIII_E25	**76,7**	5,6E-06
YPK_3889	*hmuR*	TonB-dependent heme/hemoglobin receptor family protein	YPIII_E25	**26,7**	1,4E-06
YPK_3890	*hmuS*	haemin-degrading family protein	YPIII_E25	**5,5**	2,7E-03
YPK_3891	*hmuT*	periplasmic binding protein	YPIII_E25	**5,8**	6,1E-03
YPK_3892	*hmuU*	transport system permease protein	YPIII_E25	**4,9**	4,8E-05
YPK_4073	*btuB*	TonB-dependent vitamin B12 receptor	YPIII_E25	**4,0**	2,4E-06
YPK_1001	*cynT, can*	carbonic anhydrase	YPIII_E37	**4,6**	3,0E-02
YPK_1355	*yfgD*	arsenate reductase	YPIII_E37	**3,3**	1,1E-04
YPK_1375	*afuA, fbpA*	extracellular solute-binding protein family 1	YPIII_E37	**184,9**	3,0E-38
YPK_1376	*afuB, fbpB*	binding-protein-dependent transport systems inner membrane component	YPIII_E37	**71,1**	9,3E-43
YPK_1377	*afuC*	ABC transporter related	YPIII_E37	**49,5**	3,5E-10
YPK_1378	*ydeN*	sulfatase	YPIII_E37	**8,6**	8,0E-06
YPK_1408	*cysP*	sulfate ABC transporter, periplasmic sulfate-binding protein	YPIII_E37	**2,8**	1,7E-02
YPK_1409	*cysT*	sulfate ABC transporter, inner membrane subunit	YPIII_E37	**3,8**	3,6E-02
YPK_2171	*ydcS*	extracellular solute-binding protein family 1	YPIII_E37	**5,3**	1,7E-02
YPK_2278	*ycjP-1*	binding-protein-dependent transport systems inner membrane component	YPIII_E37		4,8E-02
YPK_2438	*ftnA*	ferroxidase	YPIII_E37	**7,3**	7,0E-11
YPK_2866	*ynjE, sseA*	rhodanese domain protein	YPIII_E37	**2,1**	1,5E-02
YPK_3011	*gltJ*	polar amino acid ABC transporter, inner membrane subunit	YPIII_E37	**3,6**	3,5E-03
YPK_3441	*cysI*	sulfite reductase (NADPH) hemoprotein, beta-component	YPIII_E37	**5,0**	5,1E-10
YPK_3442	*cysJ*	sulfite reductase (NADPH) flavoprotein, alpha chain	YPIII_E37	**7,4**	8,8E-10
General membrane transport, secretion and structural proteins					
YPK_0303	*secY*	preprotein translocase, SecY subunit	YPIII_E25	**3,3**	3,9E-10
YPK_0333	*secE*	preprotein translocase, SecE subunit	YPIII_E25	**2,4**	8,0E-05
YPK_0672	*exbB*	tonB-system energizer ExbB	YPIII_E25	**7,2**	2,0E-18
YPK_0673	*exbD*	TonB system transport protein ExbD	YPIII_E25	**11,5**	9,4E-11
YPK_1831	*pmrH*	DegT/DnrJ/EryC1/StrS aminotransferase	YPIII_E25	**2,5**	4,3E-03
YPK_1833	*pmrI*	NAD-dependent epimerase/dehydratase	YPIII_E25	**2,3**	3,9E-04
YPK_1835	*arnT*	glycosyl transferase family 39	YPIII_E25	**2,2**	1,3E-02
YPK_2055	*tonB*	TonB family protein	YPIII_E25	**7,5**	1,5E-17
YPK_2649	*ompF*	porin Gram-negative type	YPIII_E25	**31,4**	9,2E-54
YPK_3263	*yajC*	preprotein translocase, YajC subunit	YPIII_E25	**2,0**	1,6E-03
YPK_3360	*ydiY*	protein of unknown function DUF481	YPIII_E25	**2,5**	3,9E-04
YPK_3733	*secG*	preprotein translocase, SecG subunit	YPIII_E25	**2,2**	3,4E-04
YPK_3957	*yfdV*	auxin efflux carrier	YPIII_E25	**2,6**	3,2E-02
YPK_0473	tccC	insecticidal toxin complex protein TccC	YPIII_E37	**4,3**	1,8E-03
YPK_1816	*mltE*	lytic transglycosylase catalytic	YPIII_E37	**2,9**	7,9E-06
YPK_2022	*osmB*	osmotically inducible lipoprotein B precursor	YPIII_E37	**3,8**	2,7E-05
YPK_2049	*ompW*	OmpW family protein	YPIII_E37	**10,2**	1,1E-02
YPK_2098	*mipA, yiaT*	MltA-interacting MipA family protein	YPIII_E37	**2,2**	1,3E-03
YPK_2224	*ompC-1*	porin Gram-negative type	YPIII_E37	**3,1**	1,6E-02
YPK_2508		mandelate racemase/muconate lactonizing protein	YPIII_E37	**3,8**	4,2E-04
YPK_2839	*ompC-2*	porin Gram-negative type	YPIII_E37	**68,3**	8,6E-67

Locus	Gene name	Gene description	Condition upregulated	Fold change	p-vale
YPK_3009	*lnt*	apolipoprotein N-acyltransferase	YPIII_E37	**2,3**	2,2E-03
YPK_3028	*tatE*	twin-arginine translocation protein, TatA/E family subunit	YPIII_E37	**4,1**	7,1E-06
YPK_3426	*nlpD*	peptidase M23B	YPIII_E37	**2,0**	4,6E-04
Defense mechanisms					
YPK_0640	*uppP*	undecaprenol kinase	YPIII_E25	**6,2**	5,6E-07
YPK_2881		HNH endonuclease	YPIII_E25	**2,7**	1,8E-04
YPK_3476	*yadH*	ABC-2 type transporter	YPIII_E25	**2,2**	8,7E-03
YPK_1648	*csy-3*	CRISPR-associated protein, Csy3 family	YPIII_E37	**2,3**	3,5E-02
YPK_1760	*cwlA, xlyA, xlyB*	N-acetylmuramyl-L-alanine amidase, negative regulator of AmpC, AmpD	YPIII_E37	**3,3**	1,7E-03
YPK_3143		putative restriction endonuclease	YPIII_E37	**2,2**	1,7E-02
Others, phage-associated					
YPK_0025	*yiaF*	putative lipoprotein	YPIII_E25	**2,3**	3,6E-03
YPK_0123	*yhiN*	HI0933 family protein	YPIII_E25	**2,2**	2,8E-03
YPK_0883		CI repressor	YPIII_E25	**3,1**	3,8E-03
YPK_1450		putative lipoprotein	YPIII_E25	**3,5**	3,9E-02
YPK_1808		2-deoxyglucose-6-phosphatase	YPIII_E25	**2,5**	2,0E-03
YPK_1952		putative virulence factor	YPIII_E25	**32,9**	6,0E-15
YPK_2249		YHS domain protein	YPIII_E25	**3,8**	3,7E-02
YPK_2989		CopG domain protein DNA-binding domain protein	YPIII_E25	**2,7**	4,5E-03
YPK_3987	*yhhQ*	conserved hypothetical integral membrane protein	YPIII_E25	**3,6**	1,8E-02
YPK_0462	*yedY*	oxidoreductase molybdopterin binding	YPIII_E37	**6,2**	7,5E-14
YPK_0661	*mdaB*	putative modulator of drug activity	YPIII_E37	**2,2**	1,7E-03
YPK_0667	*dkgA-1*	2,5-didehydrogluconate reductase	YPIII_E37	**3,4**	2,7E-04
YPK_1323		inhibitor of vertebrate lysozyme	YPIII_E37	**9,0**	1,2E-06
YPK_1586		protein RhiA	YPIII_E37	**9,3**	2,2E-02
YPK_1780	*pqiA*	paraquat-inducible protein A	YPIII_E37	**2,8**	3,2E-03
YPK_1805	*kdgF*	pectin degradation protein	YPIII_E37	**3,3**	9,3E-03
YPK_2108	*spoVR*	SpoVR family protein	YPIII_E37	**2,4**	2,1E-02
YPK_2362		Kelch repeat-containing protein	YPIII_E37	**2,0**	1,6E-02
YPK_2627		hypothetical membrane protein	YPIII_E37	**2,3**	2,7E-04
YPK_3216	*ybaY*	putative lipoprotein	YPIII_E37	**2,4**	1,1E-02
YPK_3228	*ybaW*	thioesterase superfamily protein	YPIII_E37	**2,8**	9,0E-03
YPK_3655	*yneC*	antibiotic biosynthesis monooxygenase	YPIII_E37	**43,2**	2,8E-06
YPK_3711		heparinase II/III family protein	YPIII_E37	**5,1**	4,2E-04
YPK_3768		AIG2 family protein	YPIII_E37	**2,1**	3,1E-04
Hypothetical					
YPK_0024		hypothetical protein YPK_0024	YPIII_E25	**4,4**	3,2E-02
YPK_0029		hypothetical protein YPK_0029	YPIII_E25	**2,6**	4,6E-02
YPK_0132		conserved hypothetical protein	YPIII_E25	**8,9**	1,2E-03
YPK_0633		hypothetical protein YPK_0633	YPIII_E25	**6,2**	4,5E-03
YPK_0822	*yggL*	protein of unknown function DUF469	YPIII_E25	**2,3**	6,9E-04
YPK_0844		hypothetical protein YPK_0844	YPIII_E25	**2,5**	1,7E-03
YPK_0894		hypothetical protein YPK_0894	YPIII_E25	**2,3**	4,6E-02
YPK_1053		hypothetical protein	YPIII_E25	**2,4**	8,3E-03
YPK_1434		conserved hypothetical protein	YPIII_E25	**4,2**	2,1E-02
YPK_1451		hypothetical protein	YPIII_E25	**3,8**	2,8E-02
YPK_1667		conserved hypothetical protein	YPIII_E25	**3,7**	3,2E-03
YPK_1668	*yceA*	hypothetical protein	YPIII_E25	**3,3**	1,1E-05
YPK_1681	*yceD*	protein of unknown function DUF177	YPIII_E25	**3,1**	2,8E-08
YPK_1769		conserved hypothetical protein	YPIII_E25	**3,3**	8,0E-03
YPK_1947		conserved hypothetical protein	YPIII_E25	**6,2**	3,5E-07
YPK_1954		conserved hypothetical protein	YPIII_E25	**33,2**	8,6E-43
YPK_2025		conserved hypothetical protein	YPIII_E25	**2,6**	8,2E-03
YPK_2034		conserved hypothetical protein	YPIII_E25	**3,7**	2,9E-04
YPK_2113		conserved hypothetical protein	YPIII_E25	**2,7**	2,9E-04
YPK_2146		protein of unknown function DUF28	YPIII_E25	**2,9**	4,7E-06
YPK_2357		conserved hypothetical protein	YPIII_E25	**2,3**	6,7E-04
YPK_2359		conserved hypothetical protein	YPIII_E25	**4,8**	1,2E-02
YPK_2379		conserved hypothetical protein	YPIII_E25	**98,5**	1,5E-06
YPK_2397		conserved hypothetical protein	YPIII_E25		1,8E-13
YPK_2518		conserved hypothetical protein	YPIII_E25	**8,1**	3,6E-14
YPK_2731		conserved hypothetical protein	YPIII_E25	**2,5**	2,9E-04
YPK_2781		conserved hypothetical protein	YPIII_E25	**137,0**	8,3E-29
YPK_2797	*yejL*	protein of unknown function DUF1414	YPIII_E25	**2,2**	1,4E-03
YPK_2859		conserved hypothetical protein	YPIII_E25	**2,2**	4,5E-02
YPK_2874		protein of unknown function DUF1456	YPIII_E25	**2,0**	1,7E-02
YPK_3025	*ybeD*	protein of unknown function DUF493	YPIII_E25	**2,0**	3,1E-02
YPK_3034		conserved hypothetical protein	YPIII_E25	**2,9**	2,3E-02
YPK_3162		hypothetical protein	YPIII_E25	**8,4**	1,3E-07
YPK_3236		conserved hypothetical protein	YPIII_E25	**2,4**	2,1E-05
YPK_3285		conserved hypothetical protein	YPIII_E25	**3,5**	2,3E-07
YPK_3350	*yfiH*	protein of unknown function DUF152	YPIII_E25	**2,4**	1,6E-02
YPK_3481	*yacC*	conserved hypothetical protein	YPIII_E25	**2,9**	2,3E-04
YPK_3567		conserved hypothetical protein	YPIII_E25	**2,3**	4,4E-02
YPK_3579		conserved hypothetical protein	YPIII_E25	**3,1**	2,5E-02
YPK_3580	*yjjP*	protein of unknown function DUF1212	YPIII_E25	**5,0**	1,4E-04
YPK_3637		hypothetical protein	YPIII_E25		4,6E-02
YPK_3785		conserved hypothetical protein	YPIII_E25	**5,4**	2,8E-09
YPK_4039		conserved hypothetical protein	YPIII_E25	**3,7**	1,0E-04
YPK_4107		conserved hypothetical protein	YPIII_E25	**3,9**	1,9E-02
YPK_4247	*yidD*	protein of unknown function DUF37	YPIII_E25	**2,1**	1,7E-03
pYV0026		hypothetical protein	YPIII_E37	**2,2**	3,4E-03
pYV0027		hypothetical protein	YPIII_E37	**2,3**	1,4E-06
YPK_0128		protein of unknown function DUF1498	YPIII_E37	**4,0**	2,9E-02
YPK_0440		conserved hypothetical protein	YPIII_E37	**2,2**	3,6E-03
YPK_0547		protein of unknown function DUF883 ElaB	YPIII_E37	**2,0**	2,5E-04
YPK_0576		protein of unknown function DUF1436	YPIII_E37	**2,5**	2,5E-02
YPK_0579		conserved hypothetical protein	YPIII_E37		2,1E-04
YPK_0581		conserved hypothetical protein	YPIII_E37	**2,8**	2,7E-03
YPK_0601		conserved hypothetical protein	YPIII_E37	**13,1**	1,1E-04

Locus	Gene name	Gene description	Condition upregulated	Fold change	p-vale
YPK_0856	*yggE*	protein of unknown function DUF541	YPIII_E37	**2,3**	1,1E-04
YPK_1056	*ygdH*	conserved hypothetical protein	YPIII_E37	**2,2**	3,2E-04
YPK_1186		conserved hypothetical protein	YPIII_E37	**7,6**	2,1E-02
YPK_1267		hypothetical protein YPK_1267	YPIII_E37	**8,8**	1,7E-02
YPK_1322		conserved hypothetical protein	YPIII_E37	**2,2**	1,9E-03
YPK_1507		conserved hypothetical protein	YPIII_E37	**2,5**	3,5E-02
YPK_1574		conserved hypothetical protein	YPIII_E37	**2,9**	1,7E-03
YPK_1653		hypothetical protein YPK_1653	YPIII_E37	**7,7**	2,4E-06
YPK_1731		conserved hypothetical protein	YPIII_E37	**7,3**	3,8E-14
YPK_1842	*ppsR*	protein of unknown function DUF299	YPIII_E37	**5,6**	2,2E-05
YPK_1901		conserved hypothetical protein	YPIII_E37	**2,1**	9,9E-04
YPK_1989		hypothetical protein YPK_1989	YPIII_E37	**2,7**	9,7E-04
YPK_1990		conserved hypothetical protein	YPIII_E37	**3,3**	1,4E-05
YPK_2058		conserved hypothetical protein	YPIII_E37	**10,6**	3,8E-03
YPK_2059		conserved hypothetical protein	YPIII_E37	**4,5**	1,5E-02
YPK_2094	*yeaC*	protein of unknown function DUF1315	YPIII_E37	**2,5**	2,0E-04
YPK_2185		conserved hypothetical protein	YPIII_E37	**6,7**	4,0E-06
YPK_2196		conserved hypothetical protein	YPIII_E37	**2,5**	1,8E-02
YPK_2197		conserved hypothetical protein	YPIII_E37	**42,4**	4,6E-28
YPK_2198		conserved hypothetical protein	YPIII_E37	**39,6**	1,4E-24
YPK_2199		conserved hypothetical protein	YPIII_E37	**228,3**	1,5E-43
YPK_2200		hypothetical protein YPK_2200	YPIII_E37	**1319,2**	8,7E-14
YPK_2507		conserved hypothetical protein	YPIII_E37	**3,3**	6,6E-04
YPK_2646		hypothetical protein YPK_2646	YPIII_E37	**3,0**	1,1E-03
YPK_2653		protein of unknown function DUF882	YPIII_E37	**2,9**	4,9E-06
YPK_2663		protein of unknown function DUF1338	YPIII_E37	**3,3**	1,9E-02
YPK_2804		conserved hypothetical protein	YPIII_E37	**10,0**	2,2E-06
YPK_2837		protein of unknown function DUF1348	YPIII_E37	**3,6**	7,8E-04
YPK_3014		protein of unknown function DUF1451	YPIII_E37	**2,6**	4,2E-04
YPK_3029		conserved hypothetical protein	YPIII_E37	**2,4**	1,9E-02
YPK_3087		conserved hypothetical protein	YPIII_E37	**2,3**	2,0E-02
YPK_3097		conserved hypothetical protein	YPIII_E37	**2,1**	5,0E-04
YPK_3119		hypothetical protein YPK_3119	YPIII_E37	**2,7**	4,1E-04
YPK_3145		conserved hypothetical protein	YPIII_E37	**2,0**	3,2E-02
YPK_3203		conserved hypothetical protein	YPIII_E37	**2,8**	1,0E-03
YPK_3281	*yaiE*	protein of unknown function DUF1255	YPIII_E37	**2,1**	1,6E-03
YPK_3310		conserved hypothetical protein	YPIII_E37	**6,6**	7,2E-03
YPK_3333		conserved hypothetical protein	YPIII_E37	**3,4**	4,8E-03
YPK_3656		conserved hypothetical protein	YPIII_E37	**2,4**	6,7E-03
YPK_3710		conserved hypothetical protein	YPIII_E37	**3,4**	2,9E-02
YPK_3773		protein of unknown function DUF1107	YPIII_E37	**16,2**	4,9E-26
YPK_3774	*ytfJ*	conserved hypothetical protein	YPIII_E37	**6,1**	1,9E-06
YPK_3922		protein of unknown function DUF485	YPIII_E37	**119,2**	6,2E-06
YPK_4004		conserved hypothetical protein	YPIII_E37	**31,4**	2,2E-40
YPK_4005		protein of unknown function UPF0261	YPIII_E37	**38,1**	7,7E-37
YPK_4163		hypothetical protein YPK_4163	YPIII_E37	**2,2**	2,2E-03

Table S 9: Influence of Crp on the gene expression at 25°C. Indicated are all differentially regulated genes with the fold change given to the condition in which the gene was upregulated.

Locus	Gene name	Gene description	Condition upregulated	Fold change	p-value
Virulence					
pYV0024	*sycE, yerA*	putative yopE chaperone	YPIII_S25	**2,1**	4,8E-02
pYV0054	*yopD*	putative Yop negative regulation/targeting component	YPIII_S25	**2,9**	2,6E-03
pYV0076	*lcrF, virF*	putative thermoregulatory protein	YPIII_S25	**4,3**	2,2E-02
YPK_0280	*bfd*	BFD domain protein (2Fe-2S)-binding domain protein	YPIII_S25	**2,6**	1,4E-02
YPK_0736	*slyB-1*	17 kDa surface antigen	YPIII_S25	**5,3**	8,7E-03
YPK_0792	*yspI*	autoinducer synthesis protein	YPIII_S25	**17,4**	4,9E-06
YPK_1656	*ypsI*	autoinducer synthesis protein	YPIII_S25	**9,8**	6,6E-03
YPK_1705	*ycfJ*	17 kDa surface antigen	YPIII_S25	**16,2**	7,2E-06
YPK_1786	*fimA-3*	fimbrial protein	YPIII_S25	**3,1**	1,4E-02
YPK_1876	*rovA*	transcriptional regulator, MarR family	YPIII_S25	**18,3**	8,2E-08
YPK_1953	*srfB*	putative virulence factor SrfB	YPIII_S25		2,1E-02
YPK_2156	*hlyA*	filamentous haemagglutinin domain protein	YPIII_S25	**3,2**	8,7E-03
YPK_2429	*invA*	invasin region 3	YPIII_S25	**28,5**	4,0E-16
YPK_2758	*psaB*	pili assembly chaperone	YPIII_S25	**54,5**	1,0E-04
YPK_2759	*psaA*	pH 6 antigen precursor (antigen 4) (adhesin)	YPIII_S25	**45,1**	4,7E-11
YPK_2760	*psaF*	conserved hypothetical protein	YPIII_S25	**61,9**	6,1E-08
YPK_2761	*psaE*	transcriptional regulator, CadC	YPIII_S25	**57,6**	1,2E-10
YPK_3060	*yhhZ-2*	type VI secretion system effector, Hcp1 family	YPIII_S25	**7,2**	3,7E-02
YPK_3653	*lsrB*	autoinducer AI-2 ABC transporter, periplasmic AI-2-binding protein	YPIII_S25	**11,3**	2,5E-02
pYV0072	*yscS*	putative type III secretion protein	crp_S25	**4,3**	3,6E-02
pYV0084	*yscH*	yscH, yopR, lcrP; putative type III secretion protein	crp_S25	**3,4**	1,4E-03
YPK_0051	*fimA-1*	fimbrial protein	crp_S25	**111,8**	1,3E-32
YPK_0052	*yqiG*	fimbrial biogenesis outer membrane usher protein	crp_S25	**6,7**	2,3E-03
YPK_0054		fimbrial protein	crp_S25	**8,9**	2,7E-02
YPK_0385	*hcp1-1*	type VI secretion system effector, Hcp1 family	crp_S25	**9,2**	1,8E-03
YPK_0387	*impC-1*	type VI secretion protein, EvpB/VC_A0108 family	crp_S25	**4,1**	1,5E-02
YPK_1268	*ailA*	virulence-related outer membrane protein	crp_S25	**2,8**	5,9E-03
YPK_1606	*ompX/ailD*	virulence-related outer membrane protein	crp_S25	**11,8**	1,0E-10
YPK_1761	*yadE*	YadA domain protein	crp_S25	**42,9**	1,1E-31
YPK_2615	*cnfy*	cytotoxic necrotizing factor	crp_S25	**3,4**	5,7E-03
YPK_3550	*icmF*	type VI secretion protein IcmF	crp_S25	**28,1**	4,9E-20
YPK_3551		type IV / VI secretion system protein, DotU family	crp_S25	**92,0**	5,5E-21
YPK_3552		type VI secretion protein, VC_A0114 family	crp_S25	**73,5**	3,1E-21

Locus	Gene name	Gene description	Condition upregulated	Fold change	p-value
YPK_3556		pentapeptide repeat protein	crp_S25	**88,1**	1,6E-15
YPK_3557		pentapeptide repeat protein	crp_S25	**78,9**	1,9E-23
YPK_3558	*vgrG*	type VI secretion system Vgr family protein	crp_S25	**82,2**	1,4E-26
YPK_3559	*clpB*	type VI secretion ATPase, ClpV1 family	crp_S25	**80,9**	1,1E-29
YPK_3560	*impH-2, vasB-2*	type VI secretion protein, VC_A0111 family	crp_S25	**57,4**	8,1E-18
YPK_3561	*impG-2, vasA-2*	type VI secretion protein, VC_A0110 family	crp_S25	**51,9**	1,2E-26
YPK_3562	*impH-3*	type VI secretion system lysozyme-related protein	crp_S25	**90,6**	5,7E-26
YPK_3563	*impC-2*	protein of unknown function DUF796	crp_S25	**48,8**	5,9E-36
YPK_3564	*impC-3*	type VI secretion protein, EvpB/VC_A0108 family	crp_S25	**27,7**	3,6E-23
YPK_3565		type VI secretion protein, VC_A0107 family	crp_S25	**65,1**	5,6E-30
YPK_3566		ImpA domain protein	crp_S25	**81,7**	4,8E-30
YPK_3799	*hfq*	RNA chaperone Hfq	crp_S25	**2,2**	1,9E-02
YPK_4109	*raxA*	secretion protein HlyD family protein	crp_S25	**15,1**	1,9E-02
Cell motility and chemotaxis					
YPK_1037	*ppdA*	prepilin peptidase dependent protein A	YPIII_S25	**25,9**	1,0E-06
YPK_1348	*fliB*	protein of unknown function UPF0153	YPIII_S25	**10,4**	1,9E-02
YPK_1745	*flhD*	flagellar transcriptional activator	YPIII_S25	**73,1**	8,3E-20
YPK_1746	*flhC*	flagellar transcriptional activator FlhC	YPIII_S25	**37,1**	1,3E-13
YPK_1747	*motA*	chemotaxis protein MotA	YPIII_S25	**48,9**	4,1E-08
YPK_1748	*motB*	OmpA/MotB domain protein	YPIII_S25	**19,4**	5,6E-05
YPK_1749	*cheA*	CheA signal transduction histidine kinase	YPIII_S25	**7,9**	7,9E-04
YPK_1750	*cheW*	CheW protein	YPIII_S25	**8,5**	2,1E-02
YPK_1753	*cheD*	methyl-accepting chemotaxis sensory transducer	YPIII_S25	**7,5**	1,1E-02
YPK_2380	*fliA*	RNA polymerase, sigma 28 subunit, FliA/WhiG	YPIII_S25		2,8E-03
YPK_2381	*fliC*	flagellin domain protein	YPIII_S25	**8,7**	1,5E-04
YPK_2382	*fliD*	flagellar hook-associated 2 domain protein	YPIII_S25	**6,1**	2,4E-02
YPK_2376	*fliY*	extracellular solute-binding protein family 3	crp_S25	**3,0**	6,2E-03
Stress adaptation					
YPK_0120	*uspA*	UspA domain protein	YPIII_S25	**8,7**	1,1E-08
YPK_0564	*hdeD*	acid-resistance membrane protein	YPIII_S25	**5,0**	7,1E-06
YPK_2017	*cstA-1*	carbon starvation protein CstA	YPIII_S25	**46,3**	3,3E-12
YPK_2694	*cspD-2*	cold-shock DNA-binding domain protein	YPIII_S25	**17,2**	3,9E-07
YPK_3031	*cspE*	cold-shock DNA-binding domain protein	YPIII_S25	**7,4**	8,0E-04
YPK_0175	*hslO*	Hsp33 protein	crp_S25	**4,3**	1,1E-02
YPK_0526	*sspA*	glutathione S-transferase domain	crp_S25	**2,3**	1,1E-02
YPK_3269	*ggt*	gamma-glutamyltransferase	crp_S25	**14,4**	8,6E-11
YPK_3445	*sodC*	superoxide dismutase	crp_S25	**5,5**	1,6E-05
YPK_3823	*groES*	chaperonin Cpn10	crp_S25	**2,3**	2,3E-02
Information storage and processing					
Replication, cell division					
pYV0017		putative resolvase	YPIII_S25	**2,8**	1,3E-02
YPK_3668		integrase family protein	YPIII_S25		7,4E-03
YPK_0465	*mreB*	cell shape determining protein, MreB/Mrl family	crp_S25	**2,9**	1,6E-02
YPK_1041	*recC*	exodeoxyribonuclease V, gamma subunit	crp_S25	**2,5**	1,0E-02
YPK_1043	*RecB*	exodeoxyribonuclease V, beta subunit	crp_S25	**2,7**	4,5E-03
YPK_1044	*RecD*	exodeoxyribonuclease V, alpha subunit	crp_S25	**4,1**	2,7E-02
YPK_2488		serine/threonine protein kinase involved in cell cycle control	crp_S25	**5,0**	2,0E-05
YPK_2667	*ihfB*	integration host factor, beta subunit	crp_S25	**2,3**	3,3E-02
YPK_3231	*hupB*	histone family protein DNA-binding protein	crp_S25	**2,6**	4,0E-02
YPK_3508	*mutT*	mutator MutT protein	crp_S25	**4,0**	1,2E-02
General transcription, transcription factors, signal transduction					
YPK_0248	*crp*	transcriptional regulator, Crp/Fnr family	YPIII_S25	**42,4**	1,9E-16
YPK_0367	*iclR*	transcriptional regulator, IclR family	YPIII_S25	**3,3**	5,2E-03
YPK_0533	*arcB*	multi-sensor hybrid histidine kinase	YPIII_S25	**2,2**	1,9E-02
YPK_0979		transcriptional regulator, LacI family	YPIII_S25	**7,7**	4,9E-02
YPK_1270	*csiE*	stationary phase inducible protein CsiE	YPIII_S25	**6,3**	1,2E-03
YPK_1384	*narP*	two component transcriptional regulator, LuxR family	YPIII_S25	**3,4**	2,4E-02
YPK_1614	*lacI, galR*	transcriptional regulator, LacI family	YPIII_S25	**8,2**	9,1E-03
YPK_1975		GAF modulated sigma54 specific transcriptional regulator, Fis family	YPIII_S25	**5,0**	2,3E-04
YPK_1981	*mlc*	ROK family protein	YPIII_S25	**6,2**	5,6E-04
YPK_1982	*ynfL*	transcriptional regulator, LysR family	YPIII_S25	**4,0**	3,7E-03
YPK_1996	*araC*	transcriptional regulator, AraC family	YPIII_S25	**4,3**	1,7E-03
YPK_2074	*hns*	histone family protein nucleoid-structuring protein H-NS	YPIII_S25	**5,5**	4,8E-06
YPK_3358	*yehT; ypdB*	two component transcriptional regulator, LytTR family	YPIII_S25	**10,3**	3,0E-03
YPK_3397	*fucR*	transcriptional regulator, DeoR family	YPIII_S25		1,6E-07
YPK_3661		transcriptional regulator, AraC family	YPIII_S25	**6,3**	3,7E-02
YPK_3760	*sfsB*	putative transcriptional regulator, Nlp	YPIII_S25	**9,2**	1,7E-03
YPK_3841	*rhaR*	transcriptional regulator, AraC family	YPIII_S25	**38,5**	4,0E-05
YPK_3859	*zur*	zinc uptake transcriptional repressor	YPIII_S25	**2,7**	1,4E-02
YPK_0308	*rpoA*	DNA-directed RNA polymerase, alpha subunit	crp_S25	**4,7**	3,6E-06
YPK_0340	*rpoB*	DNA-directed RNA polymerase, beta subunit	crp_S25	**2,2**	1,7E-02
YPK_0341	*rpoC*	DNA-directed RNA polymerase, beta' subunit	crp_S25	**3,0**	8,1E-04
YPK_0452	*fis*	transcriptional regulator, Fis family	crp_S25	**10,7**	1,7E-07
YPK_0516	*mlaB*	putative anti-sigma B factor antagonist	crp_S25	**11,2**	9,8E-08
YPK_0517		BolA family protein	crp_S25	**2,6**	2,4E-02
YPK_1292	*yfgA*	transcriptional regulator, XRE family	crp_S25	**3,1**	4,3E-03
YPK_2166		putative transcriptional regulator	crp_S25	**3,1**	4,5E-02
YPK_2221	*hutC*	transcriptional regulator, histidine utilization repressor, GntR family	crp_S25	**11,2**	6,6E-03
YPK_2356	*uvrY*	two component transcriptional regulator, LuxR family	crp_S25	**2,9**	2,1E-02
YPK_2470	*atoS1*	diguanylate cyclase with PAS/PAC sensor	crp_S25	**7,4**	3,0E-05
YPK_3368	*luxS*	quorum-sensing autoinducer 2 (AI-2), LuxS	crp_S25	**4,4**	2,2E-05
YPK_3425	*rpoS*	RNA polymerase, sigma 70 subunit, RpoD family	crp_S25	**2,6**	1,0E-02
YPK_3449	*relA*	(p)ppGpp synthetase I, SpoT/RelA	crp_S25	**4,7**	2,4E-05
YPK_3632	*osmY*	hyperosmotically inducible periplasmic protein	crp_S25	**2,7**	1,9E-02
YPK_3976	*rpoH*	RNA polymerase, sigma 32 subunit, RpoH	crp_S25	**2,8**	1,7E-03
YPK_4034	*rho*	transcription termination factor Rho	crp_S25	**2,5**	3,9E-02
YPK_4177	*rpoZ*	DNA-directed RNA polymerase, omega subunit	crp_S25	**2,2**	2,6E-02
YPK_4178	*spoT*	(p)ppGpp synthetase I, SpoT/RelA	crp_S25	**2,5**	2,3E-02
YPK_4184		thioesterase domain protein	crp_S25	**9,0**	4,7E-03

Locus	Gene name	Gene description	Condition upregulated	Fold change	p-value
Translation					
YPK_0311	*arfA*	alternative ribosome-rescue factor	YPIII_S25	**3,2**	3,3E-02
YPK_1084	*tilS*	tRNA(Ile)-lysidine synthetase	YPIII_S25	**2,7**	3,2E-02
YPK_3353	*yfiA*	sigma 54 modulation protein/ribosomal protein S30EA	YPIII_S25	**3,3**	1,1E-03
YPK_0149	*glgC*	glucose-1-phosphate adenylyltransferase	crp_S25	**2,3**	2,2E-02
YPK_0275	*rpsL*	30S ribosomal protein S12	crp_S25	**2,0**	3,8E-02
YPK_0276	*rpsG*	ribosomal protein S7	crp_S25	**2,5**	4,5E-03
YPK_0277	*fusA*	translation elongation factor G	crp_S25	**2,6**	8,2E-03
YPK_0282	*rpsJ*	ribosomal protein S10	crp_S25	**5,8**	2,8E-04
YPK_0283	*rplC*	ribosomal protein L3	crp_S25	**6,0**	2,1E-05
YPK_0284	*rplD*	ribosomal protein L4/L1e	crp_S25	**4,7**	1,6E-04
YPK_0285	*rplW*	ribosomal protein L25/L23	crp_S25	**3,1**	6,7E-03
YPK_0286	*rplB*	ribosomal protein L2	crp_S25	**4,1**	1,2E-04
YPK_0287	*rpsS*	ribosomal protein S19	crp_S25	**2,6**	2,2E-02
YPK_0288	*rplV*	ribosomal protein L22	crp_S25	**5,0**	5,2E-05
YPK_0289	*rpsC*	ribosomal protein S3	crp_S25	**3,9**	7,4E-04
YPK_0290	*rplP*	ribosomal protein L16	crp_S25	**4,9**	1,0E-05
YPK_0291	*rpmC*	ribosomal protein L29	crp_S25	**5,2**	1,4E-03
YPK_0292	*rpsQ*	ribosomal protein S17	crp_S25	**3,7**	2,2E-02
YPK_0293	*rplN*	ribosomal protein L14	crp_S25	**2,5**	2,7E-02
YPK_0295	*rplE*	ribosomal protein L5	crp_S25	**2,8**	4,9E-03
YPK_0296	*rpsN*	ribosomal protein S14	crp_S25	**2,9**	1,7E-03
YPK_0298	*rplF*	ribosomal protein L6	crp_S25	**2,5**	8,7E-03
YPK_0299	*rplR*	ribosomal protein L18	crp_S25	**2,4**	2,0E-02
YPK_0300	*rpsE*	ribosomal protein S5	crp_S25	**4,0**	2,4E-04
YPK_0301	*rpmD*	ribosomal protein L30	crp_S25	**3,1**	2,1E-02
YPK_0302	*rplO*	ribosomal protein L15	crp_S25	**4,2**	9,8E-05
YPK_0304	*rpmJ*	ribosomal protein L36	crp_S25	**6,6**	1,7E-07
YPK_0305	*rpsM*	ribosomal protein S13	crp_S25	**3,6**	7,5E-04
YPK_0306	*rpsK*	ribosomal protein S11	crp_S25	**5,5**	6,1E-08
YPK_0307	*rpsD*	ribosomal protein S4	crp_S25	**4,9**	1,3E-06
YPK_0309	*rplQ*	ribosomal protein L17	crp_S25	**8,0**	2,0E-09
YPK_0453	*dusB*	tRNA-dihydrouridine synthase B	crp_S25	**2,3**	2,0E-02
YPK_0487		guanine-specific ribonuclease N1 and T1	crp_S25	**3,0**	2,1E-02
YPK_0524	*rplM*	ribosomal protein L13	crp_S25	**2,6**	9,5E-03
YPK_0525	*rpsI*	ribosomal protein S9	crp_S25	**3,0**	6,7E-04
YPK_0924	*lysS*	lysyl-tRNA synthetase	crp_S25	**2,1**	4,8E-02
YPK_1066	*rpsB*	ribosomal protein S2	crp_S25	**3,9**	1,0E-03
YPK_1067	*tsf*	translation elongation factor Ts	crp_S25	**3,7**	2,2E-03
YPK_1677	*rne*	ribonuclease, Rne/Rng family	crp_S25	**2,4**	3,9E-03
YPK_1682	*rpmF*	ribosomal protein L32	crp_S25	**3,6**	2,1E-05
YPK_1822	*rpmI*	ribosomal protein L35	crp_S25	**3,5**	2,3E-04
YPK_1823	*rplT*	ribosomal protein L20	crp_S25	**4,3**	1,7E-05
YPK_2161	*rimJ*	GCN5-related N-acetyltransferase	crp_S25	**2,8**	4,5E-02
YPK_2668	*rpsA*	ribosomal protein S1	crp_S25	**6,0**	5,4E-09
YPK_2681	*serS*	seryl-tRNA synthetase	crp_S25	**3,5**	2,2E-03
YPK_2793	*rsuA*	pseudouridine synthase	crp_S25	**2,5**	2,8E-02
YPK_3005	*miaB*	tRNA-i(6)A37 thiotransferase enzyme MiaB	crp_S25	**2,3**	2,2E-02
YPK_3015	*leuS*	leucyl-tRNA synthetase	crp_S25	**2,7**	4,4E-03
YPK_3361	*rplS*	ribosomal protein L19	crp_S25	**3,4**	6,7E-03
YPK_3362	*trmD*	tRNA (guanine-N1)-methyltransferase	crp_S25	**2,5**	1,6E-02
YPK_3435	*cysN*	sulfate adenylyltransferase, large subunit	crp_S25	**46,6**	1,6E-12
YPK_3633	*prfC*	peptide chain release factor 3	crp_S25	**2,3**	3,8E-02
YPK_3724	*deaD*	DEAD/DEAH box helicase domain protein	crp_S25	**17,4**	1,3E-18
YPK_3730	*infB*	translation initiation factor IF-2	crp_S25	**2,4**	3,2E-02
YPK_3756	*rpmA*	ribosomal protein L27	crp_S25	**2,6**	1,8E-03
YPK_4154	*rpmB*	ribosomal protein L28	crp_S25	**2,4**	2,6E-02
YPK_4185	*dtd*	D-tyrosyl-tRNA(Tyr) deacylase	crp_S25	**4,2**	1,5E-02
YPK_4186	*rbn*	ribonuclease BN	crp_S25	**8,8**	1,7E-05
YPK_4188	*bipA*	GTP-binding protein TypA	crp_S25	**2,1**	2,2E-02
Posttranslational modification, protein turnover					
YPK_0242	*ppiA*	peptidyl-prolyl cis-trans isomerase cyclophilin type	YPIII_S25	**7,9**	2,0E-02
YPK_1878	*anmK*	anhydro-N-acetylmuramic acid kinase	YPIII_S25	**5,1**	8,1E-03
YPK_2095	*msrB*	methionine-R-sulfoxide reductase	YPIII_S25	**2,8**	2,3E-02
YPK_1042	*ptrA*	peptidase M16 domain protein	crp_S25	**5,0**	6,7E-06
YPK_1137	*ureD*	Urease accessory protein UreD	crp_S25	**4,4**	9,0E-03
YPK_3452	*htrA*	protease Do	crp_S25	**2,5**	5,6E-03
YPK_3571	*surA*	SurA domain	crp_S25	**2,3**	2,1E-02
YPK_3594	*dnaK*	chaperone protein DnaK	crp_S25	**2,4**	2,3E-02
YPK_3621	*radA*	DNA repair protein RadA	crp_S25	**2,8**	4,5E-02
YPK_3795	*hflC*	HflC protein	crp_S25	**2,6**	2,5E-03
YPK_3796	*hflK*	HflK protein	crp_S25	**2,8**	1,1E-02
YPK_3863	*ubiA*	4-hydroxybenzoate polyprenyl transferase	crp_S25	**5,0**	7,4E-03
Metabolism					
Energy production and conversion					
YPK_0152	*glpD*	FAD dependent oxidoreductase	YPIII_S25	**8,3**	2,4E-02
YPK_0558	*sstT*	sodium:dicarboxylate symporter	YPIII_S25	**14,1**	1,2E-10
YPK_0600		Na+/H+ antiporter NhaC	YPIII_S25	**5,9**	1,7E-02
YPK_1441		aldo/keto reductase	YPIII_S25	**6,6**	2,1E-03
YPK_2771	*gabD-2*	aldehyde dehydrogenase	YPIII_S25	**3,3**	1,2E-02
YPK_2966	*sucC*	succinyl-CoA synthetase, beta subunit	YPIII_S25	**2,3**	2,3E-02
YPK_2968	*kgd*	2-oxoglutarate dehydrogenase, E1 subunit	YPIII_S25	**2,1**	4,6E-02
YPK_2969	*sdhB*	succinate dehydrogenase and fumarate reductase iron-sulfur protein	YPIII_S25	**4,0**	4,6E-04
YPK_2970	*sdhA*	succinate dehydrogenase, flavoprotein subunit	YPIII_S25	**2,9**	3,8E-03
YPK_2972	*sdhC*	succinate dehydrogenase, cytochrome b556 subunit	YPIII_S25	**4,2**	2,3E-04
YPK_2990	*fldA*	flavodoxin	YPIII_S25	**2,5**	3,8E-02
YPK_3049	*mmsA, iolA*	methylmalonate-semialdehyde dehydrogenase	YPIII_S25	**12,7**	6,5E-05
YPK_3192	*ddhD*	oxidoreductase FAD/NAD(P)-binding domain protein	YPIII_S25	**2,9**	2,0E-02
YPK_3241	*cyoA*	ubiquinol oxidase, subunit II	YPIII_S25	**2,7**	6,1E-03
YPK_3300	*nqrF*	NADH:ubiquinone oxidoreductase, subunit F	YPIII_S25	**2,7**	4,8E-02
YPK_3303	*nqrC*	NADH:ubiquinone oxidoreductase, subunit C	YPIII_S25	**6,0**	1,1E-03

Locus	Gene name	Gene description	Condition upregulated	Fold change	p-value
YPK_3305	*nqrA*	NADH:ubiquinone oxidoreductase, subunit A	YPIII_S25	**3,4**	9,7E-03
YPK_3343	*yfiQ*	GCN5-related N-acetyltransferase	YPIII_S25	**3,2**	2,6E-03
YPK_3404	*fumA*	hydro-lyase, Fe-S type, tartrate/fumarate subfamily, beta subunit	YPIII_S25	**2,9**	3,4E-03
YPK_3761	*mdh*	malate dehydrogenase, NAD-dependent	YPIII_S25	**5,3**	3,8E-05
YPK_3813	*frdA*	fumarate reductase, flavoprotein subunit	YPIII_S25	**3,3**	1,2E-02
YPK_3814	*frdB*	succinate dehydrogenase and fumarate reductase iron-sulfur protein	YPIII_S25	**4,4**	7,8E-04
YPK_3815	*frdC*	fumarate reductase subunit C	YPIII_S25	**2,8**	2,2E-02
YPK_3816	*frdD*	fumarate reductase D subunit	YPIII_S25	**2,7**	4,8E-02
YPK_0174	*pckA*	phosphoenolpyruvate carboxykinase (ATP)	crp_S25	**3,4**	1,3E-04
YPK_0235	*nirB*	nitrite reductase (NAD(P)H), large subunit	crp_S25	**3,2**	3,6E-02
YPK_0864	*ubiH*	2-polyprenyl-6-methoxyphenol 4-hydroxylase	crp_S25	**3,5**	7,3E-03
YPK_1181	*nadB*	L-aspartate oxidase	crp_S25	**7,0**	5,2E-09
YPK_2227	*astD*	succinylglutamic semialdehyde dehydrogenase	crp_S25	**2,2**	2,4E-02
YPK_3489	*lpdA*	dihydrolipoamide dehydrogenase	crp_S25	**2,8**	1,3E-02
YPK_3885	*hemN-2*	coproporphyrinogen dehydrogenase	crp_S25	**4,8**	1,9E-02
YPK_4091	*ppc*	phosphoenolpyruvate carboxylase	crp_S25	**6,0**	1,5E-04
Carbohydrate transport and metabolism					
YPK_0057	*xylF*	D-xylose ABC transporter, periplasmic substrate-binding protein	YPIII_S25		1,5E-02
YPK_0241	*celF*	glycoside hydrolase family 4	YPIII_S25	**4,7**	3,1E-02
YPK_0431	*yphF-1, ytfQ-1*	carbohydrate uptake (CUT2 family) ABC transporter, periplasmic carbohydrate-binding protein	YPIII_S25	**8,3**	9,6E-06
YPK_0858	*rpiA*	ribose 5-phosphate isomerase	YPIII_S25	**2,4**	3,3E-02
YPK_1145	*celB*	PTS system, lactose/cellobiose family IIC subunit	YPIII_S25	**4,6**	3,2E-03
YPK_1273	*suhB*	inositol-phosphate phosphatase	YPIII_S25	**6,9**	2,4E-02
YPK_1444	*glk*	glucokinase	YPIII_S25	**3,2**	2,0E-02
YPK_1999	*araF*	monosaccharide-transporting ATPase	YPIII_S25	**5,5**	2,1E-02
YPK_2464	*manX*	PTS system, mannose/fructose/sorbose family, IIB subunit	YPIII_S25	**2,0**	4,2E-02
YPK_2496		TRAP dicarboxylate transporter, DctP subunit	YPIII_S25	**6,3**	3,4E-02
YPK_2502		polysaccharide deacetylase	YPIII_S25	**39,0**	2,0E-08
YPK_2566	*mglB*	periplasmic binding protein/LacI transcriptional regulator	YPIII_S25	**36,8**	1,3E-15
YPK_2762	*fruA*	PTS system, fructose subfamily, IIC subunit	YPIII_S25	**11,1**	2,5E-06
YPK_2763	*fruK*	1-phosphofructokinase	YPIII_S25	**24,9**	1,3E-03
YPK_2764	*fruB*	phosphocarrier, HPr family	YPIII_S25	**18,3**	8,9E-04
YPK_2778	*uxuA*	mannonate dehydratase	YPIII_S25	**4,2**	1,9E-03
YPK_2996	*nagE*	PTS system, N-acetylglucosamine-specific IIBC subunit	YPIII_S25	**4,2**	2,1E-03
YPK_3040	*iolE*	xylose isomerase domain protein TIM barrel	YPIII_S25	**4,6**	3,4E-02
YPK_3041	*iolC*	ribokinase-like domain-containing protein	YPIII_S25	**6,1**	1,1E-03
YPK_3045	*rbsB-4*	monosaccharide-transporting ATPase	YPIII_S25	**17,9**	1,8E-07
YPK_3046	*iolG*	inositol 2-dehydrogenase	YPIII_S25	**42,1**	2,9E-06
YPK_3395	*araD-2*	L-ribulose-5-phosphate 4-epimerase	YPIII_S25	**33,3**	1,3E-02
YPK_3398	*yphF-5, ytfQ-5*	carbohydrate uptake ABC transporter 2 (CUT2) family, periplasmic carbohydrate-binding protein	YPIII_S25	**13,0**	2,6E-02
YPK_3639	*ybhC*	pectinesterase	YPIII_S25	**16,8**	2,4E-05
YPK_3707	*ycjP*	binding-protein-dependent transport systems inner membrane component	YPIII_S25	**19,0**	1,2E-04
YPK_3709	*ycjN*	extracellular solute-binding protein family 1	YPIII_S25	**24,8**	6,7E-04
YPK_4210	*rbsD*	RbsD or FucU transport	YPIII_S25	**34,4**	1,8E-14
YPK_0093	*bcsZ*	endo-1,4-D-glucanase	crp_S25	**2,3**	3,2E-02
YPK_0147	*glgB*	1,4-alpha-glucan branching enzyme	crp_S25	**2,1**	1,3E-02
YPK_0148	*glgX*	glycogen debranching enzyme GlgX	crp_S25	**2,1**	4,5E-02
YPK_0150	*glgA*	glycogen/starch synthase, ADP-glucose type	crp_S25	**3,8**	2,9E-04
YPK_0151	*glgP-1*	glycogen/starch/alpha-glucan phosphorylase	crp_S25	**6,0**	7,3E-09
YPK_0247		integral membrane protein, YccS/YhfK family	crp_S25	**3,3**	3,5E-03
YPK_0373	*pgi*	glucose-6-phosphate isomerase	crp_S25	**2,4**	1,4E-02
YPK_0376	*malG*	binding-protein-dependent transport systems inner membrane component	crp_S25	**11,0**	6,7E-08
YPK_0494	*treC*	alpha,alpha-phosphotrehalase	crp_S25	**21,2**	3,6E-12
YPK_0495	*treB*	PTS system, trehalose-specific IIBC subunit	crp_S25	**13,8**	3,4E-13
YPK_0502	*yhbJ*	glmZ(sRNA)-inactivating NTPase, glucosamine-6-phosphate regulated	crp_S25	**2,5**	3,3E-02
YPK_0853	*fbaA*	fructose-bisphosphate aldolase, class II	crp_S25	**2,1**	3,4E-02
YPK_1034	*ptsP*	PTSINtr with GAF domain, PtsP	crp_S25	**2,5**	1,6E-02
YPK_1811	*yniA*	fructosamine kinase	crp_S25	**5,1**	4,1E-06
YPK_1855	*pykF*	pyruvate kinase	crp_S25	**5,4**	3,2E-06
YPK_3271	*malZ*	alpha amylase catalytic region	crp_S25	**15,9**	3,9E-09
YPK_3371	*yqaB*	beta-phosphoglucomutase family hydrolase	crp_S25	**7,3**	7,3E-05
YPK_3446	*eno*	phosphopyruvate hydratase	crp_S25	**4,1**	3,5E-05
YPK_3491	*aceE*	2-oxo-acid dehydrogenase E1 subunit, homodimeric type	crp_S25	**2,3**	3,1E-02
YPK_3599	*talB*	transaldolase	crp_S25	**2,4**	1,2E-02
YPK_3625	*deoB*	phosphopentomutase	crp_S25	**3,6**	3,6E-03
YPK_3734	*glmM*	phosphoglucosamine mutase	crp_S25	**2,5**	1,0E-02
YPK_3775	*cysQ*	3'(2'),5'-bisphosphate nucleotidase	crp_S25	**3,9**	4,2E-05
YPK_3962	*ugpB*	extracellular solute-binding protein family 1	crp_S25	**11,0**	7,2E-05
YPK_4229	*glmS*	glucosamine--fructose-6-phosphate aminotransferase, isomerizing	crp_S25	**4,1**	1,2E-03
Amino acid transport and metabolism					
pYV0007	*repB, copB*	repB, repA2, copB; putative replication transcriptional regulator	YPIII_S25	**4,0**	4,6E-02
YPK_0599		aminotransferase class I and II	YPIII_S25	**27,4**	8,5E-03
YPK_0651		glutathionylspermidine synthase	YPIII_S25	**3,4**	5,1E-03
YPK_0966	*xltA*	ABC transporter related	YPIII_S25	**16,4**	6,6E-04
YPK_1417	*patB, malY*	aminotransferase class I and II	YPIII_S25	**25,7**	1,4E-02
YPK_1538	*hisJ*	cationic amino acid ABC transporter, periplasmic binding protein	YPIII_S25	**7,0**	7,2E-05
YPK_1539	*hisQ*	polar amino acid ABC transporter, inner membrane subunit	YPIII_S25	**14,7**	2,4E-03
YPK_1610	*gutB*	alcohol dehydrogenase zinc-binding domain protein	YPIII_S25	**10,7**	4,2E-02
YPK_1712	*pepT-2*	peptidase T	YPIII_S25	**3,2**	1,5E-02
YPK_1950	*ilvB*	acetolactate synthase, large subunit, biosynthetic type	YPIII_S25	**9,1**	2,2E-03
YPK_1983	*ynfM*	major facilitator superfamily MFS_1	YPIII_S25	**6,7**	5,6E-04
YPK_1998	*araG*	ABC transporter related	YPIII_S25	**5,2**	2,8E-02
YPK_2069	*oppB*	alkaline phosphatase	YPIII_S25	**3,6**	3,9E-03
YPK_2070	*oppA*	extracellular solute-binding protein family 5	YPIII_S25	**3,8**	1,0E-04
YPK_2107	*dadA*	D-amino-acid dehydrogenase	YPIII_S25	**20,4**	2,9E-10
YPK_2451	*sdaA*	L-serine dehydratase 1	YPIII_S25	**3,0**	4,7E-03
YPK_2503		major facilitator superfamily MFS_1	YPIII_S25	**15,1**	2,0E-04
YPK_2512		major facilitator superfamily MFS_1	YPIII_S25	**17,5**	1,2E-06
YPK_2564	*mglC*	monosaccharide-transporting ATPase	YPIII_S25	**8,8**	3,6E-03

Locus	Gene name	Gene description	Condition upregulated	Fold change	p-value
YPK_2565	*mglA*	ABC transporter related	YPIII_S25	**19,3**	8,9E-08
YPK_2739	*sdaC*	serine transporter	YPIII_S25	**4,8**	1,4E-02
YPK_2860	*adiA*	lysine decarboxylase	YPIII_S25	**5,9**	2,6E-04
YPK_2861	*adiC*	arginine:agmatin antiporter	YPIII_S25	**12,2**	7,1E-04
YPK_2932	*bioA*	adenosylmethionine-8-amino-7-oxononanoate aminotransferase	YPIII_S25	**34,6**	5,2E-05
YPK_3010	*ybeJ/gltI*	extracellular solute-binding protein family 3	YPIII_S25	**17,5**	5,6E-14
YPK_3012	*gltK*	polar amino acid ABC transporter, inner membrane subunit	YPIII_S25	**6,8**	3,7E-04
YPK_3013	*gltL*	ABC transporter related	YPIII_S25	**2,8**	2,0E-02
YPK_3044	*rbsA-3*	ABC transporter related	YPIII_S25	**10,2**	7,3E-05
YPK_3048	*iolD*	thiamine pyrophosphate protein domain protein TPP-binding	YPIII_S25	**9,8**	3,1E-02
YPK_3225	*cof*	Cof-like hydrolase	YPIII_S25	**2,9**	3,2E-02
YPK_3651	*ydeY*	monosaccharide-transporting ATPase	YPIII_S25		2,9E-02
YPK_3825	*aspA*	aspartate ammonia-lyase	YPIII_S25	**6,3**	2,1E-06
YPK_3923	*actP*	cation/acetate symporter ActP	YPIII_S25	**8,9**	3,0E-08
YPK_0076	*hutU*	urocanate hydratase	crp_S25	**10,3**	2,7E-05
YPK_0077	*hutH*	histidine ammonia-lyase	crp_S25	**12,1**	2,9E-05
YPK_0116	*opdA*	oligopeptidase A	crp_S25	**4,3**	3,4E-04
YPK_0225	*aroK*	shikimate kinase	crp_S25	**3,5**	1,0E-02
YPK_0512	*mlaF*	ABC transporter related	crp_S25	**3,2**	7,2E-03
YPK_0529	*gltD*	glutamate synthase, small subunit	crp_S25	**3,4**	3,8E-02
YPK_1302	*guaB*	inosine-5'-monophosphate dehydrogenase	crp_S25	**3,4**	9,0E-04
YPK_1411	*cysA*	sulfate ABC transporter, ATPase subunit	crp_S25	**11,5**	5,5E-05
YPK_1412	*cysM*	cysteine synthase B	crp_S25	**4,1**	3,0E-02
YPK_1429	*cysK*	cysteine synthase A	crp_S25	**3,9**	2,5E-04
YPK_1430	*cysZ*	putative sulfate transport protein CysZ	crp_S25	**3,5**	7,8E-04
YPK_1446	*alaC*	aminotransferase class I and II	crp_S25	**2,7**	2,0E-02
YPK_1558	*alaA*	aminotransferase class I and II	crp_S25	**3,2**	7,0E-03
YPK_1791	*yebQ*	major facilitator superfamily MFS_1	crp_S25	**2,3**	4,7E-02
YPK_2184	*prsA*	ribose-phosphate pyrophosphokinase	crp_S25	**2,9**	1,6E-02
YPK_2223	*hutG*	N-formylglutamate amidohydrolase	crp_S25	**46,8**	1,1E-04
YPK_2226	*astB*	succinylarginine dihydrolase	crp_S25	**2,2**	3,6E-02
YPK_2228	*astA*	arginine N-succinyltransferase	crp_S25	**2,7**	2,3E-02
YPK_2229	*astC*	succinylornithine transaminase family	crp_S25	**2,0**	3,1E-02
YPK_2367	*putP*	sodium/proline symporter	crp_S25	**3,5**	4,6E-02
YPK_2670	*aroA*	3-phosphoshikimate 1-carboxyvinyltransferase	crp_S25	**4,1**	3,9E-03
YPK_2671	*serC*	phosphoserine aminotransferase	crp_S25	**3,3**	2,0E-03
YPK_2752	*lysP*	amino acid permease-associated region	crp_S25	**26,9**	8,5E-20
YPK_2792	*bcr*	drug resistance transporter, Bcr/CflA subfamily	crp_S25	**2,8**	6,3E-03
YPK_2867	*ddc*	aromatic-L-amino-acid decarboxylase	crp_S25	**19,8**	1,8E-10
YPK_3436	*cysD*	sulfate adenylyltransferase, small subunit	crp_S25	**45,2**	9,3E-10
YPK_3440	*cysH*	phosphoadenosine phosphosulfate reductase	crp_S25	**7,8**	2,1E-07
YPK_3856	*qor*	alcohol dehydrogenase zinc-binding domain protein	crp_S25	**3,6**	3,0E-02
YPK_3884	*metF-1*	methylenetetrahydrofolate reductase	crp_S25	**12,4**	7,3E-07
YPK_3994	*ybhA, ybjI, yidA, yigL*	putative sugar phosphatase	crp_S25	**3,5**	3,5E-02
YPK_4088	*argB*	acetylglutamate kinase	crp_S25	**4,9**	2,1E-02
YPK_4089	*argC*	N-acetyl-gamma-glutamyl-phosphate reductase	crp_S25	**11,8**	1,1E-02
YPK_4237		extracellular solute-binding protein family 3	crp_S25	**12,1**	3,5E-08
Nucleotide transport and metabolism					
YPK_1289	*ndk*	nucleoside-diphosphate kinase	YPIII_S25	**3,1**	2,2E-02
YPK_2073	*tdk*	thymidine kinase	YPIII_S25	**8,1**	1,1E-02
YPK_1303	*guaA*	GMP synthase, large subunit	crp_S25	**3,4**	6,0E-03
YPK_1438	*nupC1*	nucleoside transporter	crp_S25	**7,8**	6,5E-06
YPK_2132	*eda*	2-dehydro-3-deoxyphosphogluconate aldolase/4-hydroxy-2-oxoglutarate aldolase	crp_S25	**3,5**	4,8E-02
YPK_2669	*cmk*	cytidylate kinase	crp_S25	**3,4**	5,2E-04
YPK_3448	*mazG*	MazG family protein	crp_S25	**4,5**	1,2E-02
YPK_3624	*deoD*	purine nucleoside phosphorylase	crp_S25	**3,1**	9,8E-03
YPK_3626	*deoA*	thymidine phosphorylase	crp_S25	**3,3**	5,2E-03
YPK_4015	*cyaA*	putative adenylate cyclase	crp_S25	**5,5**	1,0E-07
YPK_4176	*gmk*	guanylate kinase	crp_S25	**2,9**	1,2E-02
Coenzyme transport and metabolism					
YPK_2931	*bioB*	biotin synthase	YPIII_S25	**22,0**	7,2E-06
YPK_3598	*mogA*	molybdenum cofactor synthesis domain protein	YPIII_S25	**5,6**	7,7E-03
YPK_4145	*kbl*	2-amino-3-ketobutyrate coenzyme A ligase	YPIII_S25	**4,0**	3,5E-03
YPK_4209	*rbsK*	ribokinase	YPIII_S25	**10,4**	2,1E-07
YPK_0649	*ribB*	3,4-dihydroxy-2-butanone 4-phosphate synthase	crp_S25	**3,0**	2,7E-03
YPK_0860	*ygfA*	5-formyltetrahydrofolate cyclo-ligase	crp_S25	**2,7**	8,0E-03
YPK_1261	*nadE*	NAD+ synthetase	crp_S25	**2,5**	2,2E-02
YPK_3369	*gshA*	glutamate--cysteine ligase	crp_S25	**4,4**	2,3E-04
YPK_3437	*cysG*	uroporphyrin-III C-methyltransferase	crp_S25	**38,9**	1,4E-13
YPK_3763	*yhcN*	protein of unknown function DUF1471	crp_S25	**16,0**	1,6E-05
Lipid transport and metabolism					
YPK_1506	*fadL*	membrane protein involved in aromatic hydrocarbon degradation	YPIII_S25	**8,0**	4,8E-07
YPK_1508	*fadI*	acetyl-CoA C-acyltransferase FadI	YPIII_S25	**3,8**	3,2E-02
YPK_1509	*fadJ*	fatty acid oxidation complex, alpha subunit FadJ	YPIII_S25	**2,4**	4,5E-02
YPK_1976	*ydfG*	short-chain dehydrogenase/reductase SDR	YPIII_S25	**3,3**	1,0E-02
YPK_2125	*fadD-1*	AMP-dependent synthetase and ligase	YPIII_S25	**10,7**	1,7E-09
YPK_2413		short-chain dehydrogenase/reductase SDR	YPIII_S25	**10,1**	1,0E-02
YPK_3309	*fadE*	acyl-CoA dehydrogenase	YPIII_S25	**2,5**	3,5E-02
YPK_3788	*aidB*	acyl-CoA dehydrogenase domain protein	YPIII_S25	**5,7**	1,1E-05
YPK_3933	*fadB*	fatty oxidation complex, alpha subunit FadB	YPIII_S25	**29,3**	5,1E-13
YPK_3934	*fadA*	acetyl-CoA C-acyltransferase FadA	YPIII_S25	**14,0**	3,7E-07
YPK_0663	*plsC*	1-acyl-sn-glycerol-3-phosphate acyltransferase	crp_S25	**6,1**	3,8E-05
YPK_1082	*accA*	acetyl-CoA carboxylase, carboxyl transferase, alpha subunit	crp_S25	**3,9**	5,3E-03
YPK_1193	*acpS*	holo-acyl-carrier-protein synthase	crp_S25	**3,4**	2,3E-02
YPK_1293	*ispG*	1-hydroxy-2-methyl-2-(E)-butenyl 4-diphosphate synthase	crp_S25	**3,2**	2,8E-03
YPK_1685	*fabD*	malonyl CoA-acyl carrier protein transacylase	crp_S25	**4,0**	4,4E-03
YPK_1686	*fabG*	3-oxoacyl-(acyl-carrier-protein) reductase	crp_S25	**4,5**	2,5E-05
YPK_2735		membrane protein	crp_S25	**13,2**	2,2E-02
YPK_2736		undecaprenyl-diphosphatase	crp_S25	**33,3**	2,5E-04

Locus	Gene name	Gene description	Condition upregulated	Fold change	p-value
YPK_3585	*ispH*	hydroxymethylbutenyl pyrophosphate reductase	crp_S25	**2,9**	1,7E-02
Secondary metabolites biosynthesis, transport and catabolism					
YPK_2093	*pncA*	nicotinamidase	YPIII_S25	**2,7**	2,5E-02
YPK_2509		5-oxopent-3-ene-1,2,5-tricarboxylate decarboxylase	YPIII_S25	**11,7**	1,2E-04
YPK_3921	*rcs*	acetate--CoA ligase	YPIII_S25	**9,4**	1,1E-09
YPK_0513	*mlaE*	putative ABC transporter system permease protein	crp_S25	**9,4**	1,4E-04
YPK_0514	*yrbD*	mammalian cell entry related domain protein	crp_S25	**4,4**	1,4E-04
YPK_0515	*yrbC*	toluene tolerance family protein	crp_S25	**6,5**	7,4E-06
YPK_0665	*sufI*	multicopper oxidase type 3	crp_S25	**6,1**	7,1E-04
YPK_0789		intradiol ring-cleavage dioxygenase	crp_S25	**12,8**	7,4E-08
YPK_1858	*cfa*	cyclopropane-fatty-acyl-phospholipid synthase	crp_S25	**3,3**	1,0E-02
YPK_2222	*hutI*	imidazolonepropionase	crp_S25	**24,5**	2,9E-06
Inorganic ion transport and metabolism					
YPK_0778	*SLC13A2_3_5*	anion transporter	YPIII_S25	**4,5**	4,4E-02
YPK_1001	*cynT, can*	carbonic anhydrase	YPIII_S25	**13,5**	1,4E-03
YPK_1375	*afuA, fbpA*	extracellular solute-binding protein family 1	YPIII_S25	**68,6**	5,9E-19
YPK_1376	*afuB, fbpB*	binding-protein-dependent transport systems inner membrane component	YPIII_S25	**21,7**	9,6E-09
YPK_1377	*afuC*	ABC transporter related	YPIII_S25	**14,3**	8,8E-08
YPK_1378	*ydeN*	sulfatase	YPIII_S25	**4,9**	1,1E-02
YPK_1496	*ccmA*	heme exporter protein CcmA	YPIII_S25	**2,6**	4,1E-02
YPK_2140	*znuA*	periplasmic solute binding protein	YPIII_S25	**2,4**	4,1E-02
YPK_2252	*efeU-1*	iron permease FTR1	YPIII_S25	**3,8**	2,7E-03
YPK_3011	*gltJ*	polar amino acid ABC transporter, inner membrane subunit	YPIII_S25	**9,4**	2,3E-06
YPK_3708	*ycjO*	binding-protein-dependent transport systems inner membrane component	YPIII_S25		4,7E-04
YPK_0698	*fepB*	periplasmic binding protein	crp_S25	**37,1**	5,4E-16
YPK_0782	*iutA*	TonB-dependent siderophore receptor	crp_S25	**21,2**	3,3E-02
YPK_1094	*metQ-1*	lipoprotein, YaeC family	crp_S25	**3,0**	2,1E-02
YPK_1408	*cysP*	sulfate ABC transporter, periplasmic sulfate-binding protein	crp_S25	**69,9**	7,8E-12
YPK_1409	*cysT*	sulfate ABC transporter, inner membrane subunit	crp_S25	**9,8**	8,8E-04
YPK_1410	*cysW*	sulfate ABC transporter, inner membrane subunit CysW	crp_S25	**23,4**	5,8E-05
YPK_2438	*ftnA*	ferroxidase	crp_S25	**4,0**	7,8E-04
YPK_2549		integral membrane protein TerC	crp_S25	**3,6**	8,7E-04
YPK_3441	*cysI*	sulfite reductase (NADPH) hemoprotein, beta-component	crp_S25	**5,1**	1,9E-05
YPK_3442	*cysJ*	sulfite reductase (NADPH) flavoprotein, alpha chain	crp_S25	**19,1**	1,0E-09
General membrane transport, secretion and structural proteins					
YPK_1792	*ogl*	oligogalacturonide lyase	YPIII_S25	**6,9**	3,7E-05
YPK_2224	*ompC-1*	porin Gram-negative type	YPIII_S25	**4,2**	2,5E-02
YPK_2649	*ompF*	porin Gram-negative type	YPIII_S25	**3,7**	3,3E-04
YPK_2784	*spr*	NLP/P60 protein	YPIII_S25	**10,3**	1,7E-07
YPK_3942	*tatA*	twin-arginine translocation protein, TatA/E family subunit	YPIII_S25	**3,1**	2,5E-03
YPK_0262	*rafQ*	glycosyl transferase family 9	crp_S25	**3,4**	1,9E-02
YPK_0303	*secY*	preprotein translocase, SecY subunit	crp_S25	**3,4**	1,1E-04
YPK_0333	*secE*	preprotein translocase, SecE subunit	crp_S25	**2,4**	4,0E-02
YPK_1074	*yaeT*	outer membrane protein assembly complex, YaeT protein	crp_S25	**2,4**	2,9E-02
YPK_1075	*ompH*	outer membrane chaperone Skp (OmpH)	crp_S25	**3,4**	2,6E-04
YPK_1076	*lpxD*	UDP-3-O-(3-hydroxymyristoyl) glucosamine N-acyltransferase	crp_S25	**2,1**	2,7E-02
YPK_1332	*yegM*	efflux transporter, RND family, MFP subunit	crp_S25	**3,7**	3,8E-02
YPK_1363	*dapX*	NlpBDapX family lipoprotein	crp_S25	**2,8**	5,9E-03
YPK_1864		NLP/P60 protein	crp_S25	**2,7**	4,1E-02
YPK_2550	*asmA*	putative assembly protein	crp_S25	**3,8**	8,8E-04
YPK_2740	*dacC*	serine-type D-Ala-D-Ala carboxypeptidase	crp_S25	**3,1**	9,7E-03
YPK_2839	*ompC-2*	porin Gram-negative type	crp_S25	**5,1**	4,3E-04
YPK_2955	*pal*	peptidoglycan-associated lipoprotein	crp_S25	**3,4**	3,0E-04
YPK_2959	*tolQ*	protein TolQ	crp_S25	**2,1**	3,6E-02
YPK_3016	*rlpB*	rare lipoprotein B	crp_S25	**3,9**	1,1E-03
YPK_3028	*tatE*	twin-arginine translocation protein, TatA/E family subunit	crp_S25	**6,4**	2,2E-04
YPK_3512	*lpxC*	UDP-3-0-acyl N-acetylglucosamine deacetylase	crp_S25	**2,3**	2,3E-02
YPK_3765	*mpl*	UDP-N-acetylmuramate	crp_S25	**2,8**	1,3E-02
Defense mechanisms					
YPK_0065	*hsdM-1*	N4/N6-methyltransferase family protein	YPIII_S25	**6,7**	2,5E-02
YPK_1644	*cas-1*	CRISPR-associated protein Cas1	YPIII_S25	**8,2**	2,8E-02
YPK_3496	*ampD*	N-acetylmuramyl-L-alanine amidase, negative regulator of AmpC, AmpD	YPIII_S25	**3,2**	4,1E-02
YPK_3672	*hsdM-2*	type I restriction-modification system, M subunit	YPIII_S25		4,1E-03
YPK_3673	*hsdS*	restriction modification system DNA specificity domain	YPIII_S25		3,8E-05
YPK_3674	*hsdR*	type I site-specific deoxyribonuclease, HsdR family	YPIII_S25		1,1E-04
YPK_2836	*ampH*	beta-lactamase	crp_S25	**6,5**	1,4E-04
YPK_3208	*acrB*	transporter, hydrophobe/amphiphile efflux-1 (HAE1) family	crp_S25	**2,1**	4,0E-02
Others, phage-associated					
YPK_0414		oxidoreductase domain protein	YPIII_S25	**36,3**	3,4E-03
YPK_0559		oxidoreductase domain protein	YPIII_S25	**3,7**	2,0E-02
YPK_1416	*yfbK*	von Willebrand factor type A	YPIII_S25	**3,4**	9,5E-04
YPK_1586		protein RhiA	YPIII_S25	**7,6**	2,7E-02
YPK_3036		antibiotic biosynthesis monooxygenase	YPIII_S25	**5,8**	7,3E-03
YPK_3042		oxidoreductase domain protein	YPIII_S25	**8,7**	2,9E-02
YPK_3091		tail assembly chaperone gp38	YPIII_S25	**4,8**	1,5E-02
YPK_3228	*ybaW*	thioesterase superfamily protein	YPIII_S25	**9,3**	2,0E-05
YPK_3438		YcfA family protein	YPIII_S25	**7,9**	2,4E-06
YPK_3983		Domain of unknown function DUF1820	YPIII_S25	**3,0**	4,5E-02
pYV0026		hypothetical protein	crp_S25	**2,8**	1,3E-02
YPK_0025	*yiaF*	putative lipoprotein	crp_S25	**11,2**	6,2E-11
YPK_0178		intracellular growth attenuator IgaA	crp_S25	**3,4**	3,2E-02
YPK_0187		phage baseplate assembly protein V	crp_S25	**2,9**	5,5E-04
YPK_0256	*yheT*	alpha/beta hydrolase fold	crp_S25	**6,1**	4,3E-02
YPK_0271		YheO domain protein	crp_S25	**2,4**	1,5E-02
YPK_0485	*yhcP*	fusaric acid resistance protein conserved region	crp_S25	**3,2**	4,1E-02
YPK_0536		transport-associated	crp_S25	**2,9**	2,4E-02
YPK_0544	*yphA, yqjF*	putative oxidoreductase	crp_S25	**2,1**	4,6E-02

Locus	Gene name	Gene description	Condition upregulated	Fold change	p-value
YPK_0661	*mdaB*	putative modulator of drug activity	crp_S25	**6,4**	6,7E-03
YPK_0667	*dkgA-1*	2,5-didehydrogluconate reductase	crp_S25	**4,0**	4,7E-03
YPK_1778		spore coat U domain protein	crp_S25	**4,0**	4,3E-02
YPK_1994	*yfeH*	putative sodium/bile acid symporter family protein	crp_S25	**2,8**	1,2E-02
YPK_2048		transport-associated	crp_S25	**2,6**	3,8E-03
YPK_2260		amidohydrolase 2	crp_S25	**2,5**	5,0E-02
YPK_2388	*doc*	death-on-curing family protein	crp_S25	**4,2**	4,6E-05
YPK_2638	*pqiB*	mammalian cell entry related domain protein	crp_S25	**3,0**	1,3E-02
YPK_2744		2OG-Fe(II) oxygenase	crp_S25		2,2E-02
YPK_2854		YfaZ family protein	crp_S25	**10,2**	1,3E-05
YPK_3120		putative bacteriophage protein	crp_S25	**8,2**	3,4E-02
YPK_3122		Mu tail sheath family protein	crp_S25	**26,0**	9,7E-06
YPK_3216	*ybaY*	putative lipoprotein	crp_S25	**5,5**	9,5E-06
YPK_3352	*yfiO*	putative lipoprotein	crp_S25	**3,4**	2,8E-03
YPK_3505	*yacG*	zinc-binding protein	crp_S25	**3,0**	1,5E-02
YPK_3553		putative lipoprotein	crp_S25	**89,2**	8,3E-15
YPK_3607	*creA*	CreA family protein	crp_S25	**6,6**	1,0E-05
YPK_4187	*yrfG-4, yigB-4, yihX-4*	HAD-superfamily hydrolase, subfamily IA, variant 3	crp_S25	**11,3**	7,6E-15
Hypothetical					
YPK_0560	*ygjP*	protein of unknown function DUF45	YPIII_S25	**5,4**	3,5E-02
YPK_0581		conserved hypothetical protein	YPIII_S25	**3,9**	4,9E-02
YPK_0732		conserved hypothetical protein	YPIII_S25	**13,7**	6,8E-04
YPK_0962		hypothetical protein	YPIII_S25	**12,5**	5,9E-04
YPK_1062		conserved hypothetical protein	YPIII_S25	**2,4**	1,5E-02
YPK_1263	*yhfZ*	conserved hypothetical protein	YPIII_S25	**9,9**	6,1E-04
YPK_1322		conserved hypothetical protein	YPIII_S25	**13,7**	6,5E-06
YPK_1326	*yegP*	protein of unknown function DUF1508	YPIII_S25	**2,5**	3,3E-03
YPK_1358		conserved hypothetical protein	YPIII_S25	**3,7**	8,3E-03
YPK_1359		conserved hypothetical protein	YPIII_S25	**16,2**	4,6E-02
YPK_1510		conserved hypothetical protein	YPIII_S25	**3,9**	3,8E-02
YPK_1601		protein of unknown function DUF218	YPIII_S25	**70,3**	7,5E-17
YPK_1657		protein of unknown function DUF6 transmembrane	YPIII_S25	**16,1**	1,7E-02
YPK_1725		conserved hypothetical protein	YPIII_S25	**2,6**	4,3E-02
YPK_1729		conserved hypothetical protein	YPIII_S25	**4,9**	6,0E-04
YPK_1731		conserved hypothetical protein	YPIII_S25	**2,7**	5,0E-02
YPK_1769		conserved hypothetical protein	YPIII_S25	**2,5**	1,3E-02
YPK_1770		conserved hypothetical protein	YPIII_S25	**24,6**	4,0E-02
YPK_1818		conserved hypothetical protein	YPIII_S25	**9,7**	2,6E-07
YPK_1842	*ppsR*	protein of unknown function DUF299	YPIII_S25	**5,0**	1,5E-02
YPK_1879		conserved hypothetical protein	YPIII_S25	**9,6**	9,8E-04
YPK_1954		conserved hypothetical protein	YPIII_S25	**7,6**	2,9E-02
YPK_1977		protein of unknown function DUF1283	YPIII_S25	**5,3**	1,1E-02
YPK_1989		hypothetical protein YPK_1989	YPIII_S25	**146,8**	3,7E-09
YPK_1990		conserved hypothetical protein	YPIII_S25	**27,4**	1,3E-13
YPK_2018		protein of unknown function DUF466	YPIII_S25	**10,5**	2,4E-04
YPK_2059		conserved hypothetical protein	YPIII_S25		1,8E-09
YPK_2185		conserved hypothetical protein	YPIII_S25	**28,3**	5,6E-18
YPK_2219	*ydjR*	protein of unknown function DUF886	YPIII_S25	**4,5**	9,4E-03
YPK_2309		conserved hypothetical protein	YPIII_S25	**5,4**	7,1E-03
YPK_2406		conserved hypothetical protein	YPIII_S25	**5,0**	1,2E-02
YPK_2441		conserved hypothetical protein	YPIII_S25	**4,0**	4,7E-03
YPK_2444	*yqfB*	protein of unknown function DUF437	YPIII_S25	**2,4**	2,3E-02
YPK_2471		conserved hypothetical protein	YPIII_S25	**49,5**	3,1E-04
YPK_2475		conserved hypothetical protein	YPIII_S25	**5,6**	1,8E-04
YPK_2483		hypothetical protein YPK_2483	YPIII_S25	**25,9**	2,0E-17
YPK_2555		conserved hypothetical protein	YPIII_S25	**4,6**	2,6E-02
YPK_2643		protein of unknown function DUF1379	YPIII_S25	**3,2**	1,3E-02
YPK_2646		hypothetical protein YPK_2646	YPIII_S25	**3,1**	4,8E-02
YPK_2663		protein of unknown function DUF1338	YPIII_S25	**6,4**	3,7E-05
YPK_2804		conserved hypothetical protein	YPIII_S25	**14,7**	2,2E-05
YPK_2806		hypothetical protein YPK_2806	YPIII_S25	**4,8**	4,3E-02
YPK_2924		protein of unknown function UPF0052 and CofD	YPIII_S25	**9,9**	2,6E-02
YPK_3034		conserved hypothetical protein	YPIII_S25	**5,7**	2,9E-02
YPK_3035		conserved hypothetical protein	YPIII_S25	**26,0**	8,8E-05
YPK_3063		hypothetical protein YPK_3063	YPIII_S25		3,6E-02
YPK_3203		conserved hypothetical protein	YPIII_S25	**7,3**	2,3E-05
YPK_3218		hypothetical protein YPK_3218	YPIII_S25	**10,5**	9,6E-03
YPK_3281	*yaiE*	protein of unknown function DUF1255	YPIII_S25	**4,3**	5,8E-03
YPK_3662		conserved hypothetical protein	YPIII_S25	**3,5**	2,6E-02
YPK_3710		conserved hypothetical protein	YPIII_S25	**42,9**	1,3E-07
YPK_3723		protein of unknown function DUF891	YPIII_S25	**2,8**	2,1E-02
YPK_3774	*ytfJ*	conserved hypothetical protein	YPIII_S25	**2,3**	3,8E-02
YPK_3922		protein of unknown function DUF485	YPIII_S25	**15,6**	2,1E-07
YPK_3956		conserved hypothetical protein	YPIII_S25	**3,6**	2,1E-03
YPK_4208		conserved hypothetical protein	YPIII_S25	**9,1**	1,0E-02
YPK_0384		hypothetical protein YPK_0384	crp_S25	**15,7**	8,2E-05
YPK_0497		conserved hypothetical protein	crp_S25	**31,9**	1,7E-19
YPK_1256		hypothetical protein YPK_1256	crp_S25	**4,4**	3,0E-02
YPK_1433	*ypeB*	conserved hypothetical protein	crp_S25	**4,9**	2,1E-02
YPK_1585	*elaB*	protein of unknown function DUF883 ElaB	crp_S25	**3,5**	1,7E-04
YPK_1681	*yceD*	protein of unknown function DUF177	crp_S25	**2,9**	1,2E-03
YPK_1738		hypothetical protein YPK_1738	crp_S25	**53,8**	8,2E-06
YPK_1762		conserved hypothetical protein	crp_S25	**6,9**	1,4E-05
YPK_1844		protein of unknown function UPF0118	crp_S25	**6,0**	3,6E-07
YPK_1909		hypothetical protein YPK_1909	crp_S25	**5,6**	7,3E-03
YPK_1951		protein of unknown function DUF1460	crp_S25	**9,1**	6,1E-09
YPK_2197		conserved hypothetical protein	crp_S25	**9,2**	9,8E-05
YPK_2198		conserved hypothetical protein	crp_S25	**5,9**	1,1E-04
YPK_2200		hypothetical protein YPK_2200	crp_S25	**5,5**	3,3E-06
YPK_2753		conserved hypothetical protein	crp_S25	**4,8**	1,0E-02
YPK_2868		conserved hypothetical protein	crp_S25	**30,0**	1,3E-15
YPK_3370	*yqaA*	conserved hypothetical protein	crp_S25	**8,6**	1,2E-04
YPK_3504	*yacF*	protein of unknown function DUF1342	crp_S25	**2,5**	2,4E-02

Locus	Gene name	Gene description	Condition upregulated	Fold change	p-value
YPK_3549		conserved hypothetical protein	crp_S25	**46,4**	7,9E-16
YPK_3554		conserved hypothetical protein	crp_S25	**19,2**	5,0E-08
YPK_3555		conserved hypothetical protein	crp_S25	**31,4**	2,9E-09
YPK_3567		conserved hypothetical protein	crp_S25	**36,5**	4,4E-28
YPK_3798		hypothetical protein YPK_3798	crp_S25	**4,3**	3,3E-02
YPK_3879		conserved hypothetical protein	crp_S25	**23,2**	1,1E-06
YPK_3880		conserved hypothetical protein	crp_S25	**13,6**	3,0E-04
YPK_3881		conserved hypothetical protein	crp_S25	**7,0**	7,4E-04
YPK_3882		hypothetical protein	crp_S25	**30,7**	4,1E-03
YPK_4063	*yifE*	protein of unknown function DUF413	crp_S25	**2,5**	4,3E-02
YPK_4107		conserved hypothetical protein	crp_S25	**27,8**	9,9E-26
YPK_4108		conserved hypothetical protein	crp_S25	**21,0**	4,9E-17

Table S 10: List of genes that were differentially regulated in the wild type and in a Δ*crp* strain grown at 37°C. The fold change is indicated for the growth condition in which the gene expression was induced

Locus	Gene name	Gene description	Condition up-regulated	Fold change	p-value
Virulence					
pYV0013	*yadA*	hypothetical protein	YPIII_S37	**3,0**	3,0E-02
pYV0040	*yopK/yopQ*	yop targeting protein yopK, yopQ	YPIII_S37	**3,5**	1,1E-03
pYV0047	*yopM*	putative targeted effector protein	YPIII_S37	**7,6**	1,3E-06
pYV0057	*lcrV*	putative V antigen, antihost protein/regulator	YPIII_S37	**2,5**	4,8E-04
pYV0089	*yscM, lcrQ*	putative type III secretion regulatory	YPIII_S37	**2,5**	1,2E-02
YPK_1490	*impF*	type VI secretion system lysozyme-related protein	YPIII_S37	**13,0**	2,3E-02
YPK_1655	*ypsR*	transcriptional regulator, LuxR family	YPIII_S37	**6,5**	2,7E-03
YPK_1705	*ycfJ*	17 kDa surface antigen	YPIII_S37	**17,0**	4,9E-06
YPK_1877	*slyB*	17 kDa surface antigen	YPIII_S37	**3,0**	4,9E-02
YPK_2761	*psaE*	transcriptional regulator, CadC	YPIII_S37	**3,7**	1,5E-03
YPK_2826		type III effector Hrp-dependent outers	YPIII_S37		5,4E-03
YPK_3214	*ymoA*	haemolysin expression modulating family protein	YPIII_S37		2,2E-03
YPK_3408	*yahD, arpA*	ShET2 enterotoxin domain protein	YPIII_S37	**7,1**	3,8E-02
YPK_4085	*HasA*	heme-binding A family protein	YPIII_S37	**15,7**	8,9E-03
pYV0001	*ypkA*	putative targeted effector protein kinase	crp_S25	**2,5**	2,1E-05
pYV0059	*lcrR*	hypothetical protein lcrR	crp_S25	**3,9**	1,6E-02
pYV0060	*lcrD, yscV*	putative membrane-bound Yop protein	crp_S25	**6,9**	1,5E-14
pYV0061	*yscY*	putative type III secretion protein	crp_S25	**5,6**	9,5E-08
pYV0063	*sycN*	putative type III secretion protein	crp_S25	**2,1**	7,6E-04
pYV0064	*tyeA*	putative Yop secretion and targeting protein	crp_S25	**2,8**	2,9E-05
pYV0067	*sctN*	putative Yops secretion ATP synthase	crp_S25	**2,6**	5,6E-06
pYV0068	*yscO*	putative type III secretion protein	crp_S25	**3,8**	8,1E-09
pYV0069	*yscP*	putative type III secretion protein	crp_S25	**2,3**	1,6E-04
pYV0070	*yscQ*	putative type III secretion protein	crp_S25	**8,7**	1,5E-17
pYV0071	*yscR*	putative Yop secretion membrane protein	crp_S25	**18,4**	7,2E-09
pYV0072	*yscS*	putative type III secretion protein	crp_S25	**2,5**	2,1E-02
pYV0073	*yscT*	putative type III secretion protein	crp_S25	**3,1**	9,1E-04
pYV0074	*yscU*	putative type III secretion protein	crp_S25	**7,6**	6,0E-09
pYV0079	*yscC*	putative type III secretion protein	crp_S25	**2,9**	1,3E-05
pYV0080	*yscD*	putative type III secretion protein	crp_S25	**3,4**	1,3E-05
pYV0082	*yscF*	putative type III secretion protein	crp_S25	**3,6**	1,9E-02
pYV0084	*yscH*	yscH, yopR, lcrP; putative type III secretion protein	crp_S25	**2,7**	5,7E-05
pYV0085	*yscI, lcrO*	putative type III secretion protein	crp_S25	**2,7**	5,6E-03
pYV0087	*yscK*	putative type III secretion protein	crp_S25	**3,4**	4,8E-03
YPK_1268	*ailA*	virulence-related outer membrane protein	crp_S25	**2,7**	4,4E-04
YPK_1291	*pilF*	type IV pilus biogenesis	crp_S25	**4,9**	6,5E-04
YPK_3563	*impC-2*	protein of unknown function DUF796	crp_S25	**6,3**	1,6E-02
YPK_3799	*hfq*	RNA chaperone Hfq	crp_S25	**3,4**	5,6E-03
Cell motility and chemotaxis					
YPK_1745	*flhD*	flagellar transcriptional activator	YPIII_S37		7,4E-06
YPK_1746	*flhC*	flagellar transcriptional activator FlhC	YPIII_S37		8,0E-04
Stress adaptation					
YPK_0011	*ibpA*	heat shock protein Hsp20	YPIII_S37	**2,6**	1,4E-02
YPK_0120	*uspA*	UspA domain protein	YPIII_S37	**9,8**	2,9E-11
YPK_0564	*hdeD*	acid-resistance membrane protein	YPIII_S37	**6,0**	2,1E-07
YPK_2474	*cspC-2*	cold-shock DNA-binding domain protein	YPIII_S37	**6,9**	5,9E-07
YPK_2694	*cspD-2*	cold-shock DNA-binding domain protein	YPIII_S37	**19,7**	6,6E-07
YPK_3031	*cspE*	cold-shock DNA-binding domain protein	YPIII_S37	**13,3**	7,7E-17
YPK_3161	*ybbN*	thioredoxin domain	YPIII_S37	**3,8**	2,8E-03
YPK_3877	*terZ*	stress protein	YPIII_S37	**5,5**	2,1E-02
YPK_4131	*cpxP*	protein of unknown function Spy-related	YPIII_S37	**3,2**	4,0E-03
YPK_0526	*sspA*	glutathione S-transferase domain	crp_S25	**3,5**	4,4E-02
Information storage and processing					

Locus	Gene name	Gene description	Condition up-regulated	Fold change	p-value
Replication, cell division					
pYV0032	*sopA*	putative plasmid partitioning transcription repressor	YPIII_S37	**3,3**	1,4E-04
YPK_0061		integrase family protein	YPIII_S37	**5,4**	4,3E-02
YPK_1542	*yfcH*	cell division inhibitor	YPIII_S37	**11,3**	9,6E-06
YPK_1826	*ihfA*	integration host factor, alpha subunit	YPIII_S37	**2,5**	1,3E-02
YPK_1945	*ogt*	methylated-DNA--protein-cysteine methyltransferase	YPIII_S37	**35,3**	4,5E-08
pYV0023		possible transposase remnant	crp_S25	**7,0**	3,8E-02
YPK_0465	*mreB*	cell shape determining protein, MreB/Mrl family	crp_S25	**11,9**	7,0E-06
YPK_1043	*RecB*	exodeoxyribonuclease V, beta subunit	crp_S25	**4,1**	9,1E-03
YPK_2553	*mrp*	putative ATPase Mrp	crp_S25	**3,4**	4,6E-02
YPK_2655	*mukB*	chromosome segregation and condensation protein MukB domain protein	crp_S25	**7,4**	4,0E-04
YPK_2667	*ihfB*	integration host factor, beta subunit	crp_S25	**2,0**	3,7E-02
YPK_2685	*ftsK*	cell divisionFtsK/SpoIIIE	crp_S25	**2,3**	4,2E-02
YPK_2846	*gyrA*	DNA gyrase, A subunit	crp_S25	**2,6**	4,2E-03
YPK_3144	*ybjD*	SMC (structural maintenance of chromosomes) family protein	crp_S25	**4,5**	1,3E-02
YPK_3513	*ftsZ*	cell division protein FtsZ	crp_S25	**5,5**	3,1E-06
YPK_3801	*mutL*	DNA mismatch repair protein MutL	crp_S25	**2,5**	3,8E-02
YPK_4036	*rhlB*	DEAD/DEAH box helicase domain protein	crp_S25	**2,7**	4,9E-02
General transcription, transcription factors, signal transduction					
YPK_0248	*crp*	transcriptional regulator, Crp/Fnr family	YPIII_S37	**6,3**	3,9E-03
YPK_1210		transcriptional regulator, XRE family	YPIII_S37	**7,7**	5,9E-03
YPK_1270	*csiE*	stationary phase inducible protein CsiE	YPIII_S37	**5,4**	9,9E-03
YPK_1275	*iscR*	transcriptional regulator, BadM/Rrf2 family	YPIII_S37	**2,6**	1,1E-02
YPK_1614	*lacI, galR*	transcriptional regulator, LacI family	YPIII_S37		1,1E-02
YPK_1615	*dmlR*	transcriptional regulator, LysR family	YPIII_S37	**8,3**	4,3E-02
YPK_1975		GAF modulated sigma54 specific transcriptional regulator, Fis family	YPIII_S37	**6,8**	1,7E-05
YPK_1981	*mlc*	ROK family protein	YPIII_S37	**6,0**	9,0E-03
YPK_2009		transcriptional regulator, AraC family	YPIII_S37	**3,8**	1,5E-02
YPK_2074	*hns*	histone family protein nucleoid-structuring protein H-NS	YPIII_S37	**15,6**	1,1E-07
YPK_2135	*hexR*	transcriptional regulator, RpiR family	YPIII_S37	**9,3**	7,4E-06
YPK_2491	*thuR*	transcriptional regulator, LacI family	YPIII_S37	**4,7**	3,3E-03
YPK_2738	*deoR*	transcriptional regulator, DeoR family	YPIII_S37		7,3E-04
YPK_2842	*rcsD*	phosphotransfer intermediate protein in two-component regulatory system with RcsBC	YPIII_S37	**2,8**	2,7E-03
YPK_2843	*rcsB*	two component transcriptional regulator, LuxR family	YPIII_S37	**4,7**	9,1E-05
YPK_3337	*emrR*	transcriptional regulator, MarR family	YPIII_S37	**5,7**	8,9E-04
YPK_3358	*yehT; ypdB*	two component transcriptional regulator, LytTR family	YPIII_S37		1,4E-02
YPK_3397	*fucR*	transcriptional regulator, DeoR family	YPIII_S37		1,0E-08
YPK_3841	*rhaR*	transcriptional regulator, AraC family	YPIII_S37		1,5E-02
YPK_3859	*zur*	zinc uptake transcriptional repressor	YPIII_S37	**7,4**	1,3E-02
YPK_4206		GntR domain protein	YPIII_S37	**9,1**	2,1E-02
YPK_0172	*ompR*	two component transcriptional regulator, winged helix family	crp_S25	**3,5**	3,1E-03
YPK_0173	*envZ*	integral membrane sensor signal transduction histidine kinase	crp_S25	**5,3**	4,0E-03
YPK_0308	*rpoA*	DNA-directed RNA polymerase, alpha subunit	crp_S25	**2,8**	2,5E-03
YPK_0340	*rpoB*	DNA-directed RNA polymerase, beta subunit	crp_S25	**4,3**	7,8E-05
YPK_0341	*rpoC*	DNA-directed RNA polymerase, beta' subunit	crp_S25	**3,7**	3,9E-04
YPK_0366	*aceK*	(isocitrate dehydrogenase (NADP(+))) kinase	crp_S25	**13,7**	1,5E-11
YPK_0464	*yhdA*	diguanylate cyclase/phosphodiesterase	crp_S25	**5,6**	5,6E-04
YPK_0505	*rpoN*	RNA polymerase, sigma 54 subunit, RpoN	crp_S25	**6,6**	2,4E-09
YPK_1183	*rseA*	anti sigma-E protein, RseA	crp_S25	**3,0**	5,7E-06
YPK_1184	*rseB*	sigma E regulatory protein, MucB/RseB	crp_S25	**5,4**	2,3E-10
YPK_1292	*yfgA*	transcriptional regulator, XRE family	crp_S25	**4,7**	5,6E-03
YPK_1706	*mfd*	transcription-repair coupling factor	crp_S25	**3,6**	2,6E-02
YPK_1715	*phoP*	two component transcriptional regulator, winged helix family	crp_S25	**2,7**	5,2E-03
YPK_3275	*phoR*	PAS/PAC sensor signal transduction histidine kinase	crp_S25	**3,0**	2,5E-02
YPK_3368	*luxS*	quorum-sensing autoinducer 2 (AI-2), LuxS	crp_S25	**4,4**	2,7E-03
YPK_3372	*csrA*	carbon storage regulator, CsrA	crp_S25	**2,2**	3,4E-02
YPK_3425	*rpoS*	RNA polymerase, sigma 70 subunit, RpoD family	crp_S25	**4,3**	2,3E-07
YPK_3976	*rpoH*	RNA polymerase, sigma 32 subunit, RpoH	crp_S25	**3,3**	3,2E-07
YPK_4178	*spoT*	(p)ppGpp synthetase I, SpoT/RelA	crp_S25	**3,2**	2,3E-02
Translation					
YPK_0603	*tdcF*	endoribonuclease L-PSP	YPIII_S37		2,8E-04
YPK_3353	*yfiA*	sigma 54 modulation protein/ribosomal protein S30EA	YPIII_S37	**6,0**	1,7E-09
YPK_0149	*glgC*	glucose-1-phosphate adenylyltransferase	crp_S25	**5,4**	6,0E-03
YPK_0275	*rpsL*	30S ribosomal protein S12	crp_S25	**6,9**	1,3E-06
YPK_0276	*rpsG*	ribosomal protein S7	crp_S25	**5,2**	4,3E-07
YPK_0277	*fusA*	translation elongation factor G	crp_S25	**4,8**	1,6E-11
YPK_0278	*tuf-1*	translation elongation factor Tu	crp_S25	**2,3**	6,1E-04
YPK_0295	*rplE*	ribosomal protein L5	crp_S25	**2,2**	4,0E-02
YPK_0296	*rpsN*	ribosomal protein S14	crp_S25	**2,2**	4,3E-02
YPK_0298	*rplF*	ribosomal protein L6	crp_S25	**10,7**	2,0E-05
YPK_0304	*rpmJ*	ribosomal protein L36	crp_S25	**5,0**	8,0E-03
YPK_0306	*rpsK*	ribosomal protein S11	crp_S25	**5,2**	8,9E-04
YPK_0307	*rpsD*	ribosomal protein S4	crp_S25	**3,2**	2,9E-03
YPK_0336	*rplA*	ribosomal protein L1	crp_S25	**2,7**	3,3E-03

Locus	Gene name	Gene description	Condition up-regulated	Fold change	p-value
YPK_0337	*rplJ*	ribosomal protein L10	crp_S25	**3,6**	1,3E-03
YPK_0487		guanine-specific ribonuclease N1 and T1	crp_S25	**4,5**	4,4E-03
YPK_0504	*yhbH*	sigma 54 modulation protein/ribosomal protein S30EA	crp_S25	**3,7**	1,6E-03
YPK_0863	*pepP*	peptidase M24	crp_S25	**3,2**	4,4E-02
YPK_0924	*lysS*	lysyl-tRNA synthetase	crp_S25	**2,5**	4,9E-02
YPK_1067	*tsf*	translation elongation factor Ts	crp_S25	**4,0**	1,6E-02
YPK_1187	*lepA*	GTP-binding protein LepA	crp_S25	**2,7**	1,9E-02
YPK_1190	*era*	GTP-binding protein Era	crp_S25	**3,3**	2,0E-02
YPK_1294	*hisS*	histidyl-tRNA synthetase	crp_S25	**2,8**	1,2E-02
YPK_1297	*engA*	small GTP-binding protein	crp_S25	**3,2**	2,5E-02
YPK_1822	*rpmI*	ribosomal protein L35	crp_S25	**2,2**	4,7E-02
YPK_1823	*rplT*	ribosomal protein L20	crp_S25	**2,4**	1,3E-02
YPK_1881	*tyrS*	tyrosyl-tRNA synthetase	crp_S25	**7,2**	1,1E-08
YPK_2554	*metG*	methionyl-tRNA synthetase	crp_S25	**2,6**	6,8E-03
YPK_2668	*rpsA*	ribosomal protein S1	crp_S25	**3,4**	1,2E-05
YPK_2977	*bamE, smpA*	outer membrane protein assembly factor BamE	crp_S25	**6,8**	5,5E-03
YPK_2994	*glnS*	glutaminyl-tRNA synthetase	crp_S25	**2,5**	4,3E-02
YPK_3015	*leuS*	leucyl-tRNA synthetase	crp_S25	**3,0**	7,9E-03
YPK_3364	*rpsP*	ribosomal protein S16	crp_S25	**21,7**	1,6E-02
YPK_3373	*alaS*	alanyl-tRNA synthetase	crp_S25	**3,6**	2,0E-02
YPK_3435	*cysN*	sulfate adenylyltransferase, large subunit	crp_S25	**9,2**	3,0E-03
YPK_3588	*ileS*	isoleucyl-tRNA synthetase	crp_S25	**4,3**	4,1E-04
YPK_3633	*prfC*	peptide chain release factor 3	crp_S25	**4,1**	6,9E-03
YPK_3681	*valS*	valyl-tRNA synthetase	crp_S25	**2,8**	3,1E-02
YPK_3724	*deaD*	DEAD/DEAH box helicase domain protein	crp_S25	**11,0**	4,6E-09
YPK_3726	*pnp*	polyribonucleotide nucleotidyltransferase	crp_S25	**3,0**	8,3E-04
YPK_4245	*trmE*	tRNA modification GTPase TrmE	crp_S25	**3,0**	3,8E-02
YPK_4249	*rpmH*	ribosomal protein L34	crp_S25	**4,4**	1,8E-05
Posttranslational modification, protein turnover					
YPK_1042	*ptrA*	peptidase M16 domain protein	crp_S25	**2,8**	3,3E-02
YPK_1850	*sufD*	FeS assembly protein SufD	crp_S25	**3,9**	4,0E-02
YPK_2164		cytoplasmic chaperone TorD family protein	crp_S25	**4,1**	1,1E-03
YPK_2683	*ycaJ*	AAA ATPase central domain protein	crp_S25	**7,3**	1,1E-02
YPK_3020	*rlmH*	rRNA large subunit methyltransferase	crp_S25	**24,4**	1,7E-12
YPK_3232	*lon*	ATP-dependent protease La	crp_S25	**2,8**	3,5E-03
YPK_3349	*clpB*	ATP-dependent chaperone ClpB	crp_S25	**2,5**	3,5E-04
YPK_3571	*surA*	SurA domain	crp_S25	**5,8**	2,6E-08
YPK_3795	*hflC*	HflC protein	crp_S25	**8,7**	1,1E-04
Metabolism					
Energy production and conversion					
YPK_0037	*fdoG-1*	molybdopterin oxidoreductase Fe4S4 region	YPIII_S37	**2,8**	2,3E-02
YPK_0174	*pckA*	phosphoenolpyruvate carboxykinase (ATP)	YPIII_S37	**4,0**	2,0E-04
YPK_0558	*sstT*	sodium:dicarboxylate symporter	YPIII_S37	**26,5**	7,8E-07
YPK_0563	*fadH*	NADH:flavin oxidoreductase/NADH oxidase	YPIII_S37	**9,8**	1,9E-03
YPK_2972	*sdhC*	succinate dehydrogenase, cytochrome b556 subunit	YPIII_S37	**4,2**	2,0E-03
YPK_3241	*cyoA*	ubiquinol oxidase, subunit II	YPIII_S37	**4,1**	1,0E-03
YPK_3242	*cyoB*	cytochrome o ubiquinol oxidase, subunit I	YPIII_S37	**3,0**	2,8E-03
YPK_3404	*fumA*	hydro-lyase, Fe-S type, tartrate/fumarate subfamily, beta subunit	YPIII_S37	**2,6**	1,9E-02
YPK_3761	*mdh*	malate dehydrogenase, NAD-dependent	YPIII_S37	**5,0**	2,8E-04
YPK_3813	*frdA*	fumarate reductase, flavoprotein subunit	YPIII_S37	**3,4**	1,3E-02
YPK_4113	*glpK*	glycerol kinase	YPIII_S37	**5,0**	1,1E-02
YPK_0114	*gor*	glutathione-disulfide reductase	crp_S25	**6,6**	2,9E-02
YPK_0364	*aceB*	malate synthase A	crp_S25	**7,3**	4,7E-13
YPK_0365	*aceA*	isocitrate lyase	crp_S25	**6,7**	1,4E-11
YPK_0486	*gabD-1*	succinic semialdehyde dehydrogenase	crp_S25	**5,5**	3,6E-07
YPK_0507	*lptA*	lipopolysaccharide transport periplasmic protein LptA	crp_S25	**5,7**	3,9E-05
YPK_0864	*ubiH*	2-polyprenyl-6-methoxyphenol 4-hydroxylase	crp_S25	**3,4**	3,9E-02
YPK_1026	*bisC*	molybdopterin oxidoreductase	crp_S25	**5,1**	4,9E-02
YPK_1181	*nadB*	L-aspartate oxidase	crp_S25	**8,5**	1,4E-07
YPK_1551	*ackA*	acetate kinase	crp_S25	**4,2**	4,4E-02
YPK_1562	*nuoD*	NADH dehydrogenase I, D subunit	crp_S25	**3,2**	3,0E-03
YPK_1563	*nuoE*	NADH-quinone oxidoreductase, E subunit	crp_S25	**4,4**	1,7E-02
YPK_1564	*nuoF*	NADH-quinone oxidoreductase, F subunit	crp_S25	**6,4**	2,9E-04
YPK_1565	*nuoG*	NADH-quinone oxidoreductase, chain G	crp_S25	**7,5**	2,0E-06
YPK_1566	*nuoH*	NADH dehydrogenase (quinone)	crp_S25	**8,7**	8,5E-03
YPK_1570	*nuoL*	proton-translocating NADH-quinone oxidoreductase, chain L	crp_S25	**11,6**	8,1E-04
YPK_3253	*dxs*	deoxyxylulose-5-phosphate synthase	crp_S25	**5,0**	4,9E-02
YPK_3490	*aceF*	pyruvate dehydrogenase complex dihydrolipoamide acetyltransferase	crp_S25	**2,6**	2,3E-02
YPK_4091	*ppc*	phosphoenolpyruvate carboxylase	crp_S25	**3,0**	3,8E-02
Carbohydrate transport and metabolism					
YPK_0241	*celF*	glycoside hydrolase family 4	YPIII_S37	**15,6**	1,1E-02
YPK_0554	*uxaC*	glucuronate isomerase	YPIII_S37	**11,5**	3,1E-04
YPK_0812	*rbsB-1*	ribose transport system substrate-binding protein	YPIII_S37		9,6E-03
YPK_1611	*rbsB-2*	monosaccharide-transporting ATPase	YPIII_S37		7,8E-09
YPK_1694	*ptsG*	PTS system, glucose-specific IIBC subunit	YPIII_S37	**16,8**	1,4E-04
YPK_1811	*yniA*	fructosamine kinase	YPIII_S37	**6,9**	1,1E-02
YPK_2566	*mglB*	periplasmic binding protein/LacI transcriptional regulator	YPIII_S37	**63,7**	6,3E-09
YPK_2778	*uxuA*	mannonate dehydratase	YPIII_S37	**11,3**	1,4E-05
YPK_2996	*nagE*	PTS system, N-acetylglucosamine-specific IIBC subunit	YPIII_S37	**4,9**	1,9E-02

Locus	Gene name	Gene description	Condition up-regulated	Fold change	p-value
YPK_3387	*rbsB-5*	periplasmic binding protein/LacI transcriptional regulator	YPIII_S37	**53,8**	1,7E-02
YPK_3398	*yphF-5, ytfQ-5*	carbohydrate uptake ABC transporter 2 (CUT2) family, periplasmic carbohydrate-binding protein	YPIII_S37		3,1E-02
YPK_3418	*dhaL*	dihydroxyacetone kinase, L subunit	YPIII_S37	**31,0**	5,9E-05
YPK_3419	*dhaK*	glycerone kinase	YPIII_S37	**32,7**	3,6E-05
YPK_3422	*rpiB-1*	sugar-phosphate isomerase, RpiB/LacA/LacB family	YPIII_S37	**19,8**	5,1E-07
YPK_3639	*ybhC*	pectinesterase	YPIII_S37	**9,2**	1,2E-02
YPK_3709	*ycjN*	extracellular solute-binding protein family 1	YPIII_S37		4,2E-02
YPK_4210	*rbsD*	RbsD or FucU transport	YPIII_S37	**17,9**	2,0E-06
YPK_0147	*glgB*	1,4-alpha-glucan branching enzyme	crp_S25	**2,1**	2,6E-02
YPK_0148	*glgX*	glycogen debranching enzyme GlgX	crp_S25	**4,2**	3,1E-03
YPK_0150	*glgA*	glycogen/starch synthase, ADP-glucose type	crp_S25	**3,6**	6,5E-03
YPK_0151	*glgP-1*	glycogen/starch/alpha-glucan phosphorylase	crp_S25	**3,7**	1,1E-07
YPK_0247		integral membrane protein, YccS/YhfK family	crp_S25	**6,4**	7,4E-04
YPK_0378	*malE*	extracellular solute-binding protein family 1	crp_S25	**5,1**	4,9E-02
YPK_0382	*malM*	maltose operon periplasmic	crp_S25	**4,3**	4,3E-02
YPK_0502	*yhbJ*	glmZ(sRNA)-inactivating NTPase, glucosamine-6-phosphate regulated	crp_S25	**4,9**	1,8E-03
YPK_0503	*ptsN*	PTS IIA-like nitrogen-regulatory protein PtsN	crp_S25	**3,8**	1,8E-02
YPK_0852	*pgk*	phosphoglycerate kinase	crp_S25	**2,0**	4,7E-02
YPK_1034	*ptsP*	PTSINtr with GAF domain, PtsP	crp_S25	**3,6**	2,6E-02
YPK_1426	*crr*	PTS system, glucose subfamily, IIA subunit	crp_S25	**2,4**	9,6E-03
YPK_3491	*aceE*	2-oxo-acid dehydrogenase E1 subunit, homodimeric type	crp_S25	**2,5**	6,8E-03
YPK_4229	*glmS*	glucosamine--fructose-6-phosphate aminotransferase, isomerizing	crp_S25	**3,9**	3,0E-03
Amino acid transport and metabolism					
pYV0007	*repB, copB*	repB, repA2, copB; putative replication transcriptional regulator	YPIII_S37	**3,1**	5,9E-05
YPK_0449		major facilitator superfamily MFS_1	YPIII_S37		3,0E-02
YPK_0762	*gntP*	gluconate transporter	YPIII_S37		4,9E-05
YPK_0966	*xltA*	ABC transporter related	YPIII_S37		1,5E-04
YPK_1063	*dapD*	2,3,4,5-tetrahydropyridine-2,6-dicarboxylate N-succinyltransferase	YPIII_S37	**5,0**	6,4E-05
YPK_1276	*iscS*	cysteine desulfurase IscS	YPIII_S37	**3,4**	2,0E-05
YPK_1538	*hisJ*	cationic amino acid ABC transporter, periplasmic binding protein	YPIII_S37	**10,7**	1,6E-04
YPK_1610	*gutB*	alcohol dehydrogenase zinc-binding domain protein	YPIII_S37		9,8E-12
YPK_1612	*rbsA-2*	ABC transporter related	YPIII_S37	**36,6**	1,1E-05
YPK_1712	*pepT-2*	peptidase T	YPIII_S37	**2,3**	3,4E-02
YPK_1918	*ldhA*	D-isomer specific 2-hydroxyacid dehydrogenase NAD-binding	YPIII_S37	**3,8**	2,9E-03
YPK_1961	*rbsA-3*	ABC transporter related	YPIII_S37	**13,4**	5,8E-05
YPK_2070	*oppA*	extracellular solute-binding protein family 5	YPIII_S37	**6,4**	3,0E-04
YPK_2107	*dadA*	D-amino-acid dehydrogenase	YPIII_S37	**21,2**	1,7E-07
YPK_2565	*mglA*	ABC transporter related	YPIII_S37	**13,3**	4,5E-02
YPK_2571	*frmA, adhC*	S-(hydroxymethyl)glutathione dehydrogenase/class III alcohol dehydrogenase	YPIII_S37	**3,2**	1,3E-02
YPK_2739	*sdaC*	serine transporter	YPIII_S37	**7,3**	3,4E-02
YPK_3010	*ybeJ/glt*	extracellular solute-binding protein family 3	YPIII_S37	**22,5**	1,9E-18
YPK_3421	*ydjJ*	alcohol dehydrogenase zinc-binding domain protein	YPIII_S37		3,3E-15
YPK_3825	*aspA*	aspartate ammonia-lyase	YPIII_S37	**10,1**	1,0E-03
YPK_4214	*asnA*	aspartate-ammonia ligase	YPIII_S37	**6,9**	3,8E-03
YPK_0042	*selA*	L-seryl-tRNA(Sec) selenium transferase	crp_S25	**11,0**	1,3E-02
YPK_0141	*asd*	aspartate-semialdehyde dehydrogenase	crp_S25	**3,6**	1,9E-02
YPK_0506	*yhbG*	ABC transporter related	crp_S25	**9,4**	7,8E-07
YPK_0530	*gltB*	glutamate synthase (ferredoxin)	crp_S25	**4,6**	7,8E-03
YPK_1127	*ddpC-1*	binding-protein-dependent transport systems inner membrane component	crp_S25		4,6E-02
YPK_1284	*pepB*	PepB aminopeptidase	crp_S25	**3,4**	1,8E-02
YPK_1302	*guaB*	inosine-5'-monophosphate dehydrogenase	crp_S25	**11,4**	2,1E-09
YPK_1429	*cysK*	cysteine synthase A	crp_S25	**2,3**	4,2E-02
YPK_1689	*pabC*	aminodeoxychorismate lyase	crp_S25	**3,9**	3,8E-02
YPK_2581	*ybiT*	ABC transporter related	crp_S25	**6,0**	2,6E-02
YPK_2640	*uup*	ABC transporter related	crp_S25	**2,8**	3,8E-02
YPK_2703	*poxB*	thiamine pyrophosphate protein TPP binding domain protein	crp_S25	**6,0**	1,9E-09
YPK_2792	*bcr*	drug resistance transporter, Bcr/CflA subfamily	crp_S25	**3,5**	8,9E-04
YPK_3436	*cysD*	sulfate adenylyltransferase, small subunit	crp_S25	**13,2**	3,1E-02
YPK_3440	*cysH*	phosphoadenosine phosphosulfate reductase	crp_S25	**4,0**	6,6E-05
YPK_3487	*acnB*	aconitate hydratase 2	crp_S25	**3,1**	2,7E-05
YPK_3618	*yjjK*	ABC transporter related	crp_S25	**3,1**	6,0E-03
YPK_3686	*ddpA-2*	extracellular solute-binding protein family 5	crp_S25	**2,5**	2,1E-02
YPK_3978	*ftsE*	type II (general) secretory pathway (IISP) family protein	crp_S25	**15,2**	1,4E-02
YPK_4090	*argE*	acetylornithine deacetylase (ArgE)	crp_S25	**8,6**	3,3E-02
Nucleotide transport and metabolism					
YPK_1289	*ndk*	nucleoside-diphosphate kinase	YPIII_S37	**4,4**	4,4E-03
YPK_0315	*fmt*	methionyl-tRNA formyltransferase	crp_S25	**4,3**	1,7E-02
YPK_0499	*pyrI*	aspartate carbamoyltransferase, regulatory subunit	crp_S25	**13,3**	2,4E-04
YPK_0500	*pyrB*	aspartate carbamoyltransferase	crp_S25	**20,0**	1,8E-06
YPK_1303	*guaA*	GMP synthase, large subunit	crp_S25	**6,3**	2,0E-03
YPK_1364	*purC*	phosphoribosylaminoimidazole-	crp_S25	**8,3**	9,1E-03

Locus	Gene name	Gene description	Condition up-regulated	Fold change	p-value
		succinocarboxamide synthase			
YPK_1438	*nupC1*	nucleoside transporter	crp_S25	**9,6**	1,2E-03
YPK_3793	*purA*	adenylosuccinate synthase	crp_S25	**2,8**	1,7E-04
YPK_4015	*cyaA*	putative adenylate cyclase	crp_S25	**5,8**	1,2E-07
Coenzyme transport and metabolism					
YPK_3598	*mogA*	molybdenum cofactor synthesis domain protein	YPIII_S37	**7,3**	8,5E-03
YPK_4209	*rbsK*	ribokinase	YPIII_S37	**4,4**	1,3E-02
YPK_0649	*ribB*	3,4-dihydroxy-2-butanone 4-phosphate synthase	crp_S25	**3,9**	6,2E-04
YPK_3437	*cysG*	uroporphyrin-III C-methyltransferase	crp_S25	**15,6**	1,5E-03
YPK_3572	*pdxA*	4-hydroxythreonine-4-phosphate dehydrogenase	crp_S25	**33,0**	3,9E-05
YPK_3763	*yhcN*	protein of unknown function DUF1471	crp_S25	**3,6**	7,2E-03
Lipid transport and metabolism					
YPK_1070	*dxr*	1-deoxy-D-xylulose 5-phosphate reductoisomerase	YPIII_S37	**4,3**	1,1E-02
YPK_1506	*fadL*	membrane protein involved in aromatic hydrocarbon degradation	YPIII_S37	**30,8**	7,6E-08
YPK_1508	*fadI*	acetyl-CoA C-acyltransferase FadI	YPIII_S37	**7,3**	1,1E-03
YPK_1509	*fadJ*	fatty acid oxidation complex, alpha subunit FadJ	YPIII_S37	**4,4**	2,5E-04
YPK_1576	*idnO*	short-chain dehydrogenase/reductase SDR	YPIII_S37		3,1E-02
YPK_2125	*fadD-1*	AMP-dependent synthetase and ligase	YPIII_S37	**8,9**	4,1E-08
YPK_2413		short-chain dehydrogenase/reductase SDR	YPIII_S37	**12,7**	3,2E-02
YPK_2510		short-chain dehydrogenase/reductase SDR	YPIII_S37		1,7E-03
YPK_2611	*fabZ-2*	beta-hydroxyacyl-(acyl-carrier-protein) dehydratase FabA/FabZ	YPIII_S37	**10,5**	4,7E-03
YPK_3309	*fadE*	acyl-CoA dehydrogenase	YPIII_S37	**7,1**	1,4E-07
YPK_3420		short-chain dehydrogenase/reductase SDR	YPIII_S37	**46,2**	7,9E-07
YPK_3933	*fadB*	fatty oxidation complex, alpha subunit FadB	YPIII_S37	**33,3**	3,6E-16
YPK_3934	*fadA*	acetyl-CoA C-acyltransferase FadA	YPIII_S37	**68,0**	1,4E-07
YPK_1293	*ispG*	1-hydroxy-2-methyl-2-(E)-butenyl 4-diphosphate synthase	crp_S25	**9,7**	4,2E-05
YPK_1924	*acpD*	NAD(P)H dehydrogenase (quinone)	crp_S25	**2,9**	4,0E-02
YPK_3585	*ispH*	hydroxymethylbutenyl pyrophosphate reductase	crp_S25	**6,0**	2,6E-02
YPK_3810	*psd*	phosphatidylserine decarboxylase	crp_S25	**5,4**	2,0E-03
YPK_3862	*pslB*	glycerol-3-phosphate O-acyltransferase	crp_S25	**3,7**	1,8E-04
Secondary metabolites biosynthesis, transport and catabolism					
YPK_1687	*acpP*	acyl carrier protein	YPIII_S37	**3,0**	4,6E-03
YPK_3921	*rcs*	acetate--CoA ligase	YPIII_S37	**4,2**	6,0E-04
Inorganic ion transport and metabolism					
YPK_1001	*cynT, can*	carbonic anhydrase	YPIII_S37	**8,4**	1,8E-02
YPK_1378	*ydeN*	sulfatase	YPIII_S37	**11,0**	3,1E-04
YPK_1492	*phnA*	alkylphosphonate utilization operon protein PhnA	YPIII_S37	**9,5**	9,5E-03
YPK_3011	*gltJ*	polar amino acid ABC transporter, inner membrane subunit	YPIII_S37	**14,0**	1,5E-02
YPK_0273	*tusC*	sulfur relay protein TusC/DsrF	crp_S25	**3,1**	7,3E-04
YPK_0274	*tusB*	sulfur relay protein TusB/DsrH	crp_S25	**8,6**	1,1E-08
YPK_1355	*yfgD*	arsenate reductase	crp_S25	**4,6**	4,5E-02
YPK_1408	*cysP*	sulfate ABC transporter, periplasmic sulfate-binding protein	crp_S25		1,6E-02
YPK_1813	*yfeC*	ABC-3 protein	crp_S25	**11,8**	4,7E-02
YPK_2140	*znuA*	periplasmic solute binding protein	crp_S25	**4,7**	5,3E-06
YPK_3441	*cysI*	sulfite reductase (NADPH) hemoprotein, beta-component	crp_S25	**3,1**	2,0E-03
YPK_3442	*cysJ*	sulfite reductase (NADPH) flavoprotein, alpha chain	crp_S25	**12,5**	4,9E-05
YPK_3574	*apaG*	ApaG domain protein	crp_S25	**11,8**	4,7E-02
YPK_4231	*pstS*	phosphate ABC transporter, periplasmic phosphate-binding protein	crp_S25	**4,6**	1,0E-02
General membrane transport, secretion and structural proteins					
YPK_1792	*ogl*	oligogalacturonide lyase	YPIII_S37	**4,4**	1,9E-03
YPK_2224	*ompC-1*	porin Gram-negative type	YPIII_S37	**7,7**	1,9E-02
YPK_2649	*ompF*	porin Gram-negative type	YPIII_S37	**5,2**	1,8E-05
YPK_2784	*spr*	NLP/P60 protein	YPIII_S37	**4,9**	3,3E-02
YPK_0303	*secY*	preprotein translocase, SecY subunit	crp_S25	**3,3**	3,0E-04
YPK_0430	*ddg*	lipid A biosynthesis lauroyl (or palmitoleoyl) acyltransferase	crp_S25		9,8E-03
YPK_1073	*rscP*	membrane-associated zinc metalloprotease	crp_S25	**2,2**	4,2E-02
YPK_1074	*yaeT*	outer membrane protein assembly complex, YaeT protein	crp_S25	**2,9**	2,1E-03
YPK_1075	*ompH*	outer membrane chaperone Skp (OmpH)	crp_S25	**3,2**	4,4E-03
YPK_1076	*lpxD*	UDP-3-O-(3-hydroxymyristoyl) glucosamine N-acyltransferase	crp_S25	**3,8**	2,2E-03
YPK_2139		peptidase M23B	crp_S25	**7,7**	5,8E-06
YPK_2664	*lpxK*	tetraacyldisaccharide 4'-kinase	crp_S25	**4,0**	5,1E-03
YPK_2954		tol-pal system protein YbgF	crp_S25	**2,7**	3,3E-02
YPK_2955	*pal*	peptidoglycan-associated lipoprotein	crp_S25	**2,4**	5,7E-03
YPK_2956	*tolB*	Tol-Pal system beta propeller repeat protein TolB	crp_S25	**2,7**	9,1E-06
YPK_2958	*tolR*	protein TolR	crp_S25	**5,6**	2,5E-02
YPK_3021	*pbpA*	penicillin-binding protein 2	crp_S25	**6,7**	1,7E-03
YPK_3426	*nlpD*	peptidase M23B	crp_S25	**3,3**	1,1E-07

Locus	Gene name	Gene description	Condition up-regulated	Fold change	p-value
YPK_3524	*ftsI*	peptidoglycan glycosyltransferase	crp_S25	**3,1**	2,9E-03
YPK_3570	*imp*	organic solvent tolerance protein	crp_S25	**6,2**	7,8E-10
YPK_3587	*lspA*	lipoprotein signal peptidase	crp_S25	**4,8**	4,7E-02
YPK_3733	*secG*	preprotein translocase, SecG subunit	crp_S25	**6,5**	3,6E-02
YPK_3765	*mpl*	UDP-N-acetylmuramate	crp_S25	**2,8**	2,7E-03
YPK_3809	*rsgA*	ribosome small subunit-dependent GTPase A	crp_S25	**3,7**	9,4E-03
YPK_3811	*bspA*	MscS Mechanosensitive ion channel	crp_S25	**18,1**	9,6E-05
YPK_4029	*rffG*	dTDP-glucose 4,6-dehydratase	crp_S25	**26,7**	4,2E-02
Defense mechanisms					
YPK_0062		conserved hypothetical protein	YPIII_S37	**9,1**	1,1E-03
YPK_1760	*cwlA, xlyA, xlyB*	N-acetylmuramyl-L-alanine amidase, negative regulator of AmpC, AmpD	YPIII_S37		2,8E-02
YPK_1794	*ybjR*	N-acetylmuramyl-L-alanine amidase, negative regulator of AmpC, AmpD	YPIII_S37	**12,4**	1,8E-05
Others, phage-associated					
YPK_0446		beta-lactamase domain protein	YPIII_S37	**21,2**	1,6E-03
YPK_0602		YheO domain protein	YPIII_S37		4,8E-04
YPK_1416	*yfbK*	von Willebrand factor type A	YPIII_S37	**6,5**	1,6E-03
YPK_2559	*yohJ*	LrgA family protein	YPIII_S37		4,8E-02
YPK_2632	*matP*	Ter macrodomain organizer matS-binding protein	YPIII_S37	**7,1**	8,7E-03
YPK_3228	*ybaW*	thioesterase superfamily protein	YPIII_S37	**11,8**	3,1E-05
YPK_3438		YcfA family protein	YPIII_S37	**5,0**	1,4E-05
pYV0005	*repA, repA1*	putative replication initiation protein	crp_S25	**4,0**	1,9E-05
YPK_0100		peptidase M16 domain protein	crp_S25	**6,7**	7,8E-09
YPK_0133	*ydiJ; yhaK; yhhW*	pirin domain protein	crp_S25	**5,5**	4,8E-02
YPK_0256	*yheT*	alpha/beta hydrolase fold	crp_S25	**12,7**	3,1E-02
YPK_0544	*yphA, yqjF*	putative oxidoreductase	crp_S25	**5,7**	3,3E-03
YPK_0622		phage/plasmid primase, P4 family	crp_S25	**3,2**	4,6E-02
YPK_0643		adenylate cyclase	crp_S25	**3,1**	3,2E-02
YPK_1323		Inhibitor of vertebrate lysozyme	crp_S25	**17,4**	1,1E-06
YPK_1870	*sepC*	Rhs family protein-like protein	crp_S25	**8,0**	6,2E-08
YPK_2960	*ybgC*	acyl-CoA thioester hydrolase YbgC	crp_S25	**2,6**	4,8E-03
YPK_3019	*ybeB*	ribosome-associated protein	crp_S25	**22,7**	9,8E-20
YPK_3216	*ybaY*	putative lipoprotein	crp_S25	**2,8**	1,1E-03
YPK_3352	*yfiO*	putative lipoprotein	crp_S25	**5,7**	3,2E-07
YPK_3677	*yjgQ*	permease YjgP/YjgQ family protein	crp_S25	**7,3**	2,0E-03
YPK_3725	*nlpI*	TPR repeat-containing protein	crp_S25	**3,2**	1,8E-05
Hypothetical					
pYV0044		hypothetical protein	YPIII_S37	**2,8**	2,1E-02
YPK_0044		conserved hypothetical protein	YPIII_S37		2,8E-02
YPK_0521	*yhcB*	protein of unknown function DUF1043	YPIII_S37	**3,3**	3,3E-02
YPK_0581		conserved hypothetical protein	YPIII_S37	**10,8**	6,6E-08
YPK_0587		conserved hypothetical protein	YPIII_S37	**4,9**	3,9E-02
YPK_0652		conserved hypothetical protein	YPIII_S37	**2,4**	4,4E-02
YPK_0956		conserved hypothetical protein	YPIII_S37	**15,0**	1,2E-02
YPK_0962		hypothetical protein	YPIII_S37	**15,7**	1,1E-02
YPK_1062		conserved hypothetical protein	YPIII_S37	**5,7**	1,2E-02
YPK_1322		conserved hypothetical protein	YPIII_S37	**8,8**	4,8E-05
YPK_1601		protein of unknown function DUF218	YPIII_S37	**25,8**	3,4E-04
YPK_1703		conserved hypothetical protein	YPIII_S37	**12,8**	3,3E-02
YPK_1731		conserved hypothetical protein	YPIII_S37	**5,4**	6,6E-08
YPK_1735	*ylaC*	conserved hypothetical protein	YPIII_S37	**6,5**	3,9E-05
YPK_1818		conserved hypothetical protein	YPIII_S37	**13,7**	1,5E-07
YPK_1901		conserved hypothetical protein	YPIII_S37	**3,2**	6,0E-04
YPK_1910		conserved hypothetical protein	YPIII_S37	**5,6**	7,5E-04
YPK_1959		hypothetical protein YPK_1959	YPIII_S37		2,8E-06
YPK_1960		conserved hypothetical protein	YPIII_S37	**31,5**	6,2E-05
YPK_1989		hypothetical protein YPK_1989	YPIII_S37		6,0E-03
YPK_1990		conserved hypothetical protein	YPIII_S37		1,1E-08
YPK_2185		conserved hypothetical protein	YPIII_S37	**11,4**	5,6E-11
YPK_2293		conserved hypothetical protein	YPIII_S37	**3,5**	4,1E-02
YPK_2405		hypothetical protein YPK_2405	YPIII_S37	**11,4**	4,4E-02
YPK_2471		conserved hypothetical protein	YPIII_S37		1,5E-02
YPK_2475		conserved hypothetical protein	YPIII_S37	**18,8**	2,7E-16
YPK_2500	*yaiL*	conserved hypothetical protein	YPIII_S37		4,2E-02
YPK_2588		conserved hypothetical protein	YPIII_S37		3,2E-04
YPK_2643		protein of unknown function DUF1379	YPIII_S37	**8,2**	2,2E-02
YPK_2663		protein of unknown function DUF1338	YPIII_S37	**7,6**	3,7E-02
YPK_2804		conserved hypothetical protein	YPIII_S37	**63,9**	5,7E-09
YPK_3035		conserved hypothetical protein	YPIII_S37	**80,2**	2,8E-09
YPK_3203		conserved hypothetical protein	YPIII_S37	**6,5**	1,5E-04
YPK_3213		conserved hypothetical protein	YPIII_S37	**31,7**	4,7E-05
YPK_3285		conserved hypothetical protein	YPIII_S37	**4,3**	7,3E-03
YPK_3439		protein of unknown function UPF0150	YPIII_S37	**3,4**	3,3E-02
YPK_3662		conserved hypothetical protein	YPIII_S37		3,8E-02
YPK_3723		protein of unknown function DUF891	YPIII_S37	**4,4**	3,3E-02
YPK_3753		hypothetical protein YPK_3753	YPIII_S37	**8,8**	1,5E-02
YPK_3956		conserved hypothetical protein	YPIII_S37	**26,1**	3,0E-04
YPK_4004		conserved hypothetical protein	YPIII_S37	**16,0**	6,4E-12
YPK_4005		protein of unknown function UPF0261	YPIII_S37	**9,8**	3,1E-09
pYV0026		hypothetical protein	crp_S25	**4,6**	1,1E-09
YPK_0546		conserved hypothetical protein	crp_S25	**3,0**	1,6E-02
YPK_0547		protein of unknown function DUF883 ElaB	crp_S25	**2,6**	5,3E-04
YPK_0856	*yggE*	protein of unknown function DUF541	crp_S25	**3,4**	3,9E-02
YPK_1295	*yfgM*	conserved hypothetical protein	crp_S25	**4,0**	8,5E-03

Locus	Gene name	Gene description	Condition up-regulated	Fold change	p-value
YPK_1326	*yegP*	protein of unknown function DUF1508	crp_S25	**4,9**	2,1E-03
YPK_1885		protein of unknown function DUF1282	crp_S25	**3,6**	4,6E-03
YPK_2200		hypothetical protein YPK_2200	crp_S25	**3,1**	1,7E-07
YPK_3433	*ygbE*	conserved hypothetical protein	crp_S25		4,6E-02
YPK_3549		conserved hypothetical protein	crp_S25		4,6E-02
YPK_3769	*ytfN*	protein of unknown function DUF490	crp_S25	**3,5**	4,4E-03
YPK_3773		protein of unknown function DUF1107	crp_S25	**2,9**	1,0E-06
YPK_3798		hypothetical protein YPK_3798	crp_S25	**46,7**	2,9E-03

Table S 11: TSS predicted form Illumina sequencing. The read number is given, if the TSS was identified in the corresponding conditions. Indicated are the reads counts normalized to 1,000,000 reads. Underlines read counts indicate, that the calculated depletion factor is ≤ 0.5 with a p-value below 0.05. Therefore, these TSS were calssified as real TSS.

tss id	strand	TSS position (+ strand)	Distance to start codon [nt]	Gene ID	name	Reads YPIII 25°C exp	Reads YPIII 25°C stat	Reads YPIII 37°C exp	Reads YPIII 37°C stat	Reads YP89 25°C stat	Reads YP89 37°C stat
YPKp_TSS_1	-	2698	31	pYV0002					418		80
YPKp_TSS_2	-	2718	51	pYV0002		40	59	70	46	36	
YPKp_TSS_3	-	3868	218	pYV0004		20	12	25			
YPKp_TSS_4	+	5772	31	pYV0006		76	16	176	692	286	18
YPKp_TSS_5	-	6288	36	pYV0007	*repB, copB*	20	26	552	225	45	54
YPKp_TSS_6	-	10669	268	pYV0013	*yadA*						22
YPKp_TSS_7	+	13832	33	pYV0017		13	60	15	23	10	12
YPKp_TSS_8	+	19088	132	pYV0023						94	
YPKp_TSS_9	-	20318	29	pYV0024	*sycE, yerA*		15	12	58		
YPKp_TSS_10	+	20455	28	pYV0025	*yopE*	169	120	312	1376	38	230
YPKp_TSS_11	-	20460	171	pYV0024	*sycE, yerA*				10		
YPKp_TSS_12	-	21843	-6	pYV0027		563	88	1691	138	1073	1111
YPKp_TSS_13	-	25278	27	pYV0032	*sopA*	47	15	36	15		12
YPKp_TSS_14	-	25520	269	pYV0032	*sopA*		27	20			
YPKp_TSS_15	-	34868	-16	pYV0047	*yopM*			16	21		
YPKp_TSS_16	-	40466	5	pYV0058	*lcrG*	32	73		534	57	170
YPKp_TSS_17	-	45282	37	pYV0065	*yopN, lcrE*	62	33	70	484	35	149
YPKp_TSS_18	-	45347	102	pYV0065	*yopN, lcrE*	14		42			
YPKp_TSS_19	+	45417	26	pYV0067	*sctN*	166	80	229	2115	170	1685
YPKp_TSS_20	+	50277	148	pYV0073	*yscT*	13	16	27	54	105	54
YPKp_TSS_21	+	52588	262	pYV0075	*virG*					185	131
YPKp_TSS_22	+	54062	201	pYV0077					15		
YPKp_TSS_23	+	54240	23	pYV0077		33	12	13			22
YPKp_TSS_24	+	61915	28	pYV0089	*yscM, lcrQ*		17	20	22		16
YPKp_TSS_25	-	65796	24	pYV0094	*yopH*		22	32	137		18
YPK_TSS_1	+	3737	35	YPK_0004	*gyrB*	26	23	16	31	28	
YPK_TSS_2	+	6376	26	YPK_0005		10					
YPK_TSS_3	+	11857	113	YPK_0011	*ibpA*	67	13		173		10
YPK_TSS_4	+	12405	259	YPK_0012	*ibpB*	19					
YPK_TSS_5	+	24842	39	YPK_0022	*glyQ*	14					
YPK_TSS_6	+	28225	122	YPK_0025	*yiaF*					23	
YPK_TSS_7	+	33740	49	YPK_0030		59		31		11	
YPK_TSS_8	-	34969	185	YPK_0031					11		
YPK_TSS_9	-	37972	185	YPK_0034	*tar*	17					
YPK_TSS_10	-	38809	55	YPK_0035	*sodA*	185	76	94		57	
YPK_TSS_11	+	40050	160	YPK_0037	*fdoG*		49	13	17		
YPK_TSS_12	+	40067	143	YPK_0037	*fdoG*	24	79	57	36	10	
YPK_TSS_13	-	40082	69	YPK_0036	*fdhD*			11			
YPK_TSS_14	+	40746	100	YPK_0038	*fdoG*				17		
YPK_TSS_15	+	44528	384	YPK_0041	*fdhE*			15			
YPK_TSS_16	+	50118	24	YPK_0044		15		12	19		
YPK_TSS_17	-	52984	73	YPK_0048	*mdfA*	34		21	10		
YPK_TSS_18	+	53633	139	YPK_0050		15	10				
YPK_TSS_19	+	71053	24	YPK_0062					39		
YPK_TSS_20	-	80575	65	YPK_0071		40					
YPK_TSS_21	+	84825	58	YPK_0076	*hutU*					13	
YPK_TSS_22	+	92225	90	YPK_0080	*yhjW*	14		10			
YPK_TSS_23	+	115855	85	YPK_0098	*dctA*	14		15			
YPK_TSS_24	-	120713	33	YPK_0102				13			
YPK_TSS_25	+	120820	79	YPK_0103		71					
YPK_TSS_26	-	138780	140	YPK_0115		13					
YPK_TSS_27	+	138880	89	YPK_0116	*opdA*	20					
YPK_TSS_28	-	144861	86	YPK_0119	*gdhA*	10			16		
YPK_TSS_29	-	145567	99	YPK_0120	*uspA*	15		26			
YPK_TSS_30	-	145713	245	YPK_0120	*uspA*		305	21	82		
YPK_TSS_31	+	145981	178	YPK_0121	*uspB*		163		21	24	
YPK_TSS_32	-	148166	-70	YPK_0122	*pitA*	70		15			
YPK_TSS_33	+	148352	-90	YPK_0123		10					
YPK_TSS_34	+	159920	-17	YPK_0132		26					
YPK_TSS_35	+	161039	86	YPK_0134	*gntR*	18		12			
YPK_TSS_36	+	166293	225	YPK_0141	*asd*	55	13	16		20	
YPK_TSS_37	-	188688	57	YPK_0146		5	7	5		8	
YPK_TSS_38	+	188954	183	YPK_0147	*glgB*		12		43	20	
YPK_TSS_39	-	200730	47	YPK_0152	*glpD*	849		17			
YPK_TSS_40	-	208577	121	YPK_0160	*malT*	46	43	33	18		
YPK_TSS_41	+	208595	179	YPK_0161	*glgP-2*		12				
YPK_TSS_42	-	214076	28	YPK_0163		28		18			

tss id	strand	TSS position (+ strand)	Distance to start codon [nt]	Gene ID	name	Reads YPIII 25°C exp	Reads YPIII 25°C stat	Reads YPIII 37°C exp	Reads YPIII 37°C stat	Reads YP89 25°C stat	Reads YP89 37°C stat
YPK_TSS_43	+	215806	36	YPK_0166			91			20	
YPK_TSS_44	-	219389	213	YPK_0169	*feoA*	10	39	10			14
YPK_TSS_45	-	222275	200	YPK_0170		4	5	8			
YPK_TSS_46	+	223228	32	YPK_0172	*ompR*	16		34			
YPK_TSS_47	-	227314	28	YPK_0174	*pckA*			42	14		
YPK_TSS_48	-	227357	71	YPK_0174	*pckA*		15				
YPK_TSS_49	-	229202	268	YPK_0176	*hslR*	13					
YPK_TSS_50	-	232249	315	YPK_0178		18	11			18	
YPK_TSS_51	-	237805	84	YPK_0186						222	
YPK_TSS_52	-	237892	171	YPK_0186		16	67		19	10	
YPK_TSS_53	-	240894	-54	YPK_0189		32	13	35	12		10
YPK_TSS_54	-	247143	74	YPK_0201					16		
YPK_TSS_55	+	255316	162	YPK_0218				17			
YPK_TSS_56	+	263223	230	YPK_0225	*aroK*	106	16	77	13	11	
YPK_TSS_57	+	263346	107	YPK_0225	*aroK*	69	11	30		21	
YPK_TSS_58	-	275470	24	YPK_0235	*nirB*					21	
YPK_TSS_59	-	283699	208	YPK_0241	*celF*			14			
YPK_TSS_60	+	283968	39	YPK_0242	*ppiA*	111		158			
YPK_TSS_61	-	291876	201	YPK_0248	*crp*	124	63	62	31	40	28
YPK_TSS_62	-	291962	287	YPK_0248	*crp*		4			5	
YPK_TSS_63	+	291986	25	YPK_0249		16		11			
YPK_TSS_64	-	302551	28	YPK_0262	*rafQ*	19		24		40	
YPK_TSS_65	+	308613	28	YPK_0268	*slyD*	40		23			
YPK_TSS_66	-	309675	34	YPK_0269			30	22	25	95	26
YPK_TSS_67	+	309844	112	YPK_0270	*fkpA*			28			
YPK_TSS_68	+	309903	53	YPK_0270	*fkpA*	92	14	60	10	26	
YPK_TSS_69	+	312342	170	YPK_0274			41	26	61	13	60
YPK_TSS_70	+	312758	179	YPK_0275	*rpsL*		24				
YPK_TSS_71	+	312856	81	YPK_0275	*rpsL*	581		179			
YPK_TSS_72	+	315973	179	YPK_0278	*tuf*	337	167	505	89	141	
YPK_TSS_73	+	318161	24	YPK_0280	*bfd*	48	46				
YPK_TSS_74	+	318436	22	YPK_0281	*bfr*		85		28	72	
YPK_TSS_75	+	319168	177	YPK_0282	*rpsJ*	26		18			
YPK_TSS_76	+	324411	74	YPK_0293	*rplN*			92			
YPK_TSS_77	+	329789	113	YPK_0304		510	43	122		99	
YPK_TSS_78	+	333186	285	YPK_0310	*zntR*					10	
YPK_TSS_79	+	333948	36	YPK_0311		15	27	18			10
YPK_TSS_80	-	334733	35	YPK_0312	*mscL*	17	19	13			
YPK_TSS_81	-	339183	38	YPK_0316	*def*		10				
YPK_TSS_82	+	340234	139	YPK_0318		20	46	20	27	18	14
YPK_TSS_83	-	343457	30	YPK_0322		25	12	45	12		
YPK_TSS_84	+	349613	29	YPK_0326	*murB*	35		37			
YPK_TSS_85	-	352685	65	YPK_0328	*coaA*	29		16			
YPK_TSS_86	+	354305	66	YPK_0332	*tuf*	259	121	650		238	
YPK_TSS_87	+	355662	144	YPK_0333	*secE*	66	25	47		77	26
YPK_TSS_88	+	356803	124	YPK_0335	*rplK*	1266	19	288			
YPK_TSS_89	+	358424	4	YPK_0337	*rplJ*		87		12		18
YPK_TSS_90	-	374969	53	YPK_0348	*rsd*		14				
YPK_TSS_91	+	378640	35	YPK_0353		20	11	28			
YPK_TSS_92	+	379310	144	YPK_0354	*hupA*	39		48			
YPK_TSS_93	+	379347	107	YPK_0354	*hupA*	290	118	318	57	22	12
YPK_TSS_94	+	391544	128	YPK_0364	*aceB*		18				
YPK_TSS_95	-	397609	40	YPK_0367	*iclR*		23		20		
YPK_TSS_96	+	397734	50	YPK_0368	*metH*	5					
YPK_TSS_97	+	407017	33	YPK_0373	*pgi*	16					
YPK_TSS_98	+	451718	494	YPK_0411			18	12	22		
YPK_TSS_99	+	468103	67	YPK_0428	*yjcE*	20		27			
YPK_TSS_100	-	472494	199	YPK_0430	*ddg*	13					
YPK_TSS_101	+	472998	104	YPK_0431	*yphF, ytfQ*	17	29	52			
YPK_TSS_102	-	483896	33	YPK_0440				18			
YPK_TSS_103	-	485535	179	YPK_0444	*cspA-3*	99	303	10	59	10	10
YPK_TSS_104	-	486389	32	YPK_0445	*pcp*	9	18			13	
YPK_TSS_105	-	486481	124	YPK_0445	*pcp*	40	27	23	22	14	
YPK_TSS_106	+	486727	106	YPK_0446			17		107		
YPK_TSS_107	+	488672	120	YPK_0448					19		
YPK_TSS_108	-	494083	32	YPK_0453	*dusB*	57	14	31			
YPK_TSS_109	-	495796	275	YPK_0454	*prmA*		11	10	16		
YPK_TSS_110	-	501230	30	YPK_0460	*aroQ*	70		84	11		
YPK_TSS_111	-	503277	95	YPK_0462	*yedY*			10			
YPK_TSS_112	+	504622	161	YPK_0464	*yhdA*		10				
YPK_TSS_113	+	506993	43	YPK_0465	*mreB*	20		27			
YPK_TSS_114	-	535761	177	YPK_0482					13		
YPK_TSS_115	+	539049	208	YPK_0486	*gabD-1*	14	43	57	29		40
YPK_TSS_116	+	542412	93	YPK_0490	*pmbA*	24		12			
YPK_TSS_117	-	542418	94	YPK_0489			10	14			
YPK_TSS_118	-	545926	77	YPK_0493	*rnk*			10			
YPK_TSS_119	-	545935	86	YPK_0493	*rnk*	19	12				
YPK_TSS_120	-	549589	216	YPK_0495	*treB*		4			231	
YPK_TSS_121	-	549641	268	YPK_0495	*treB*			23			
YPK_TSS_122	-	551606	159	YPK_0497		18	14			167	
YPK_TSS_123	-	552178	46	YPK_0498		133	25	86			
YPK_TSS_124	-	553926	245	YPK_0500	*pyrB*	26		13			
YPK_TSS_125	-	562958	98	YPK_0511	*yrbG*	20	39		27		
YPK_TSS_126	+	563087	38	YPK_0512	*mlaF*	11	14	12			
YPK_TSS_127	-	569591	-37	YPK_0519	*degS*	10					
YPK_TSS_128	-	571756	53	YPK_0521		13		15	10		
YPK_TSS_129	+	573112	256	YPK_0524	*rplM*	13					
YPK_TSS_130	+	573206	162	YPK_0524	*rplM*	177	39	92	12		
YPK_TSS_131	+	574395	182	YPK_0526	*sspA*	110	30	94		22	
YPK_TSS_132	-	583100	238	YPK_0530	*gltB*	21		10	16		
YPK_TSS_133	+	584869	23	YPK_0533	*arcB*			11	14		
YPK_TSS_134	+	587174	296	YPK_0534	*elbB*		18				

tss id	strand	TSS position (+ strand)	Distance to start codon [nt]	Gene ID	name	Reads YPIII 25°C exp	Reads YPIII 25°C stat	Reads YPIII 37°C exp	Reads YPIII 37°C stat	Reads YP89 25°C stat	Reads YP89 37°C stat
YPK_TSS_135	-	589845	218	YPK_0536					15		
YPK_TSS_136	-	592953	29	YPK_0539				10			
YPK_TSS_137	-	593522	598	YPK_0539		3	18	6	6	3	
YPK_TSS_138	+	595421	29	YPK_0542		14					
YPK_TSS_139	-	598058	117	YPK_0544			27		34		22
YPK_TSS_140	-	598086	145	YPK_0544		4	6	3	8	6	0
YPK_TSS_141	-	599259	30	YPK_0547		170	402	368	84	359	50
YPK_TSS_142	-	599774	10	YPK_0548			45			15	
YPK_TSS_143	-	599854	90	YPK_0548			59				
YPK_TSS_144	-	599884	120	YPK_0548		19		13		18	
YPK_TSS_145	-	601924	40	YPK_0551		52	39	34	10	56	
YPK_TSS_146	-	603013	86	YPK_0552	*exuR*	22	60	22	22	10	
YPK_TSS_147	-	612060	192	YPK_0558	*sstT*	32	65	67	57		
YPK_TSS_148	-	612110	242	YPK_0558	*sstT*				13		
YPK_TSS_149	-	621187	92	YPK_0563	*fadH*				33		
YPK_TSS_150	-	621919	42	YPK_0564		93	30	267	265	44	26
YPK_TSS_151	-	644292	8	YPK_0583	*yapF*		21				
YPK_TSS_152	-	663765	82	YPK_0598			10				
YPK_TSS_153	+	664406	43	YPK_0599				8			
YPK_TSS_154	+	672351	48	YPK_0608			10	10			
YPK_TSS_155	-	673189	21	YPK_0609		17	17	86	13	11	24
YPK_TSS_156	+	676595	64	YPK_0614			11	17			
YPK_TSS_157	-	685898	-47	YPK_0625			10	10		18	12
YPK_TSS_158	+	689091	35	YPK_0631			11				
YPK_TSS_159	-	693150	156	YPK_0634	*rpoD*			24			
YPK_TSS_160	-	693215	221	YPK_0634	*rpoD*	58	33	23	25	21	
YPK_TSS_161	-	693320	326	YPK_0634	*rpoD*				12		
YPK_TSS_162	-	693445	451	YPK_0634	*rpoD*		22				
YPK_TSS_163	-	693533	539	YPK_0634	*rpoD*		71		18	15	
YPK_TSS_164	-	695314	63	YPK_0636	*rpsU*	879	39	208	27		
YPK_TSS_165	-	695433	182	YPK_0636	*rpsU*	10	14				
YPK_TSS_166	+	695633	24	YPK_0637	*gcp*	18					
YPK_TSS_167	-	697552	41	YPK_0638		18					
YPK_TSS_168	+	697570	49	YPK_0639	*folB*	11		13			
YPK_TSS_169	+	698064	188	YPK_0640	*uppP*					12	
YPK_TSS_170	-	701351	27	YPK_0642	*ygiM*	14					
YPK_TSS_171	-	709451	31	YPK_0647		47	28	55	14	22	
YPK_TSS_172	+	709558	432	YPK_0649	*ribB*	443	347	268	99	65	10
YPK_TSS_173	-	714069	45	YPK_0652		103	257	92	229	65	16
YPK_TSS_174	-	715772	53	YPK_0654	*tolC*	46	2	28			
YPK_TSS_175	-	715838	119	YPK_0654	*tolC*	4	7	4	8	8	
YPK_TSS_176	-	722312	62	YPK_0661	*mdaB*	12		14			
YPK_TSS_177	+	722476	78	YPK_0662	*parC*	30		19			
YPK_TSS_178	+	724935	199	YPK_0663	*plsC*	5				3	
YPK_TSS_179	+	725097	37	YPK_0663	*plsC*	12					
YPK_TSS_180	-	732681	147	YPK_0668			12				
YPK_TSS_181	-	734618	40	YPK_0670			13				
YPK_TSS_182	+	736417	45	YPK_0672		25					
YPK_TSS_183	-	764127	46	YPK_0700			15			17	
YPK_TSS_184	+	790269	39	YPK_0732			13				
YPK_TSS_185	-	792348	44	YPK_0736	*slyB*	18	26	37	18		
YPK_TSS_186	+	796369	139	YPK_0738		12					
YPK_TSS_187	+	857937	34	YPK_0762	*gntP*				38		
YPK_TSS_188	+	881155	77	YPK_0777						10	
YPK_TSS_189	-	883281	78	YPK_0778					11		
YPK_TSS_190	-	936751	314	YPK_0819	*yggX*	31	14	38			
YPK_TSS_191	+	938045	98	YPK_0821	*trmB*	17					
YPK_TSS_192	-	959037	87	YPK_0835			10				
YPK_TSS_193	-	960153	38	YPK_0837		23					
YPK_TSS_194	-	965207	282	YPK_0843	*metK*	71					
YPK_TSS_195	+	965363	380	YPK_0844		28		18			
YPK_TSS_196	-	970589	42	YPK_0849	*ycaL, loiP*	41		31			
YPK_TSS_197	+	970799	222	YPK_0850	*tktA*	24		14			
YPK_TSS_198	+	970845	176	YPK_0850	*tktA*			17			
YPK_TSS_199	+	970987	34	YPK_0850	*tktA*	51					
YPK_TSS_200	+	973375	55	YPK_0851	*epd*	15	69	23	30		
YPK_TSS_201	+	974264	285	YPK_0852	*pgk*	15	12	13			
YPK_TSS_202	+	974440	109	YPK_0852	*pgk*	10	14	10			
YPK_TSS_203	+	979136	114	YPK_0856	*yggE*			16			
YPK_TSS_204	-	981000	31	YPK_0857	*iciA*		21			11	
YPK_TSS_205	+	981276	35	YPK_0858	*rpiA*	10	11	30	14		
YPK_TSS_206	+	982211	63	YPK_0859	*serA-1*			15			
YPK_TSS_207	-	985358	289	YPK_0861		77	56	64	22	34	
YPK_TSS_208	+	985376	30	YPK_0862		21		18			
YPK_TSS_209	+	990637	177	YPK_0867	*gcvT*	12		81			
YPK_TSS_210	+	1000794	97	YPK_0873		14					
YPK_TSS_211	-	1003479	33	YPK_0875				14			
YPK_TSS_212	+	1038254	27	YPK_0920	*xerD*	10		11	13		
YPK_TSS_213	+	1041779	233	YPK_0923	*prfB*		14				
YPK_TSS_214	+	1041800	212	YPK_0923	*prfB*	128	54	97		21	
YPK_TSS_215	-	1078179	31	YPK_0962			12		20		
YPK_TSS_216	-	1103277	26	YPK_0982	*gatY*	12					
YPK_TSS_217	+	1127643	55	YPK_1001	*cynT, can*		79				
YPK_TSS_218	+	1158291	102	YPK_1030		10	20		21	11	
YPK_TSS_219	-	1160191	130	YPK_1031	*tas*			12			
YPK_TSS_220	+	1164804	48	YPK_1035	*lgt*	28		18			
YPK_TSS_221	+	1172305	85	YPK_1042	*ptrA*			22			
YPK_TSS_222	+	1184722	32	YPK_1047	*mltA*	16		13			
YPK_TSS_223	-	1195623	30	YPK_1057	*queF*	12					
YPK_TSS_224	+	1196938	46	YPK_1059				13			
YPK_TSS_225	-	1200127	134	YPK_1063	*dapD*	11		30	10		
YPK_TSS_226	-	1203791	91	YPK_1065	*ampM*	15					

tss id	strand	TSS position (+ strand)	Distance to start codon [nt]	Gene ID	name	Reads YPIII 25°C exp	Reads YPIII 25°C stat	Reads YPIII 37°C exp	Reads YPIII 37°C stat	Reads YP89 25°C stat	Reads YP89 37°C stat
YPK_TSS_227	+	1203901	234	YPK_1066	*rpsB*	282		28			
YPK_TSS_228	+	1207634	52	YPK_1070	*dxr*	25	111	25	66		
YPK_TSS_229	+	1208942	164	YPK_1071	*uppS*		15		11	80	18
YPK_TSS_230	+	1209068	38	YPK_1071	*uppS*			46	15		
YPK_TSS_231	+	1210548	203	YPK_1073	*rscP*	32	25	42	25		28
YPK_TSS_232	+	1211798	345	YPK_1074	*yaeT*	13					
YPK_TSS_233	+	1211958	185	YPK_1074	*yaeT*	22	15				
YPK_TSS_234	+	1222785	345	YPK_1082	*accA*	21					
YPK_TSS_235	-	1227365	25	YPK_1087		39	353	22	38	215	
YPK_TSS_236	-	1227424	84	YPK_1087		28	16	27	27	17	
YPK_TSS_237	-	1231222	53	YPK_1091	*proS*	37		24			
YPK_TSS_238	-	1232413	29	YPK_1093	*rcsF*			15			
YPK_TSS_239	-	1235124	66	YPK_1096	*metN-1*	9		3			
YPK_TSS_240	+	1235220	25	YPK_1097	*gmhB*	53	21	69			
YPK_TSS_241	-	1235231	173	YPK_1096	*metN-1*	4		6			
YPK_TSS_242	+	1243560	82	YPK_1104		14	28	24	44		14
YPK_TSS_243	-	1245854	-10	YPK_1105	*mltD*	27	56	32		18	
YPK_TSS_244	+	1247954	51	YPK_1109	*dnaQ*	21	13	25	11	26	10
YPK_TSS_245	+	1250719	101	YPK_1111	*hpxB*		48	12	42	19	
YPK_TSS_246	+	1263048	178	YPK_1124	*cspB-1*	29	83		22	26	
YPK_TSS_247	+	1269604	627	YPK_1131	*ureA*		3				
YPK_TSS_248	+	1269840	391	YPK_1131	*ureA*			26			
YPK_TSS_249	-	1279446	283	YPK_1140	*hdeB*	21	94	93	15	12	
YPK_TSS_250	+	1287828	118	YPK_1151	*seqA*	13	19	15	13	15	
YPK_TSS_251	+	1309872	126	YPK_1172	*pcp*			10			
YPK_TSS_252	-	1311455	33	YPK_1173	*ung*	12		10			
YPK_TSS_253	+	1311555	219	YPK_1174	*grcA*				11		
YPK_TSS_254	+	1311696	78	YPK_1174	*grcA*	37	42	32		48	22
YPK_TSS_255	-	1315506	18	YPK_1179	*srmB*	19	15	40			
YPK_TSS_256	-	1315574	86	YPK_1179	*srmB*				19		
YPK_TSS_257	-	1318398	-8	YPK_1181	*nadB*	38	12	35		336	82
YPK_TSS_258	+	1318517	77	YPK_1182	*rpoE*	18	135	278	128		
YPK_TSS_259	+	1318974	221	YPK_1183	*rseA*		179	58	382	258	62
YPK_TSS_260	+	1322545	89	YPK_1187	*lepA*	13					
YPK_TSS_261	+	1325751	42	YPK_1189	*rnc*		15	11		13	
YPK_TSS_262	+	1328197	78	YPK_1192	*pdxJ*	11		11		23	
YPK_TSS_263	+	1334099	25	YPK_1200		12		10			
YPK_TSS_264	-	1347217	30	YPK_1216		49	15	22	23	27	
YPK_TSS_265	-	1349984	350	YPK_1221		43	109	47	74	77	
YPK_TSS_266	+	1375399	24	YPK_1251		12					
YPK_TSS_267	-	1377646	-8	YPK_1252			12				
YPK_TSS_268	+	1377803	86	YPK_1253	*purL*	14		26			
YPK_TSS_269	+	1386026	266	YPK_1258				15			
YPK_TSS_270	+	1393863	253	YPK_1265	*glyA*	50	49	48	43	10	12
YPK_TSS_271	+	1395762	59	YPK_1268	*ailA*	137	64	1883	31	29	
YPK_TSS_272	+	1396857	17	YPK_1269	*hcaT*	16					
YPK_TSS_273	-	1399423	34	YPK_1270			16		27		
YPK_TSS_274	-	1402157	37	YPK_1273	*suhB*	112	15	22			
YPK_TSS_275	+	1402213	26	YPK_1274	*trmJ*	14		15			
YPK_TSS_276	+	1403139	-34	YPK_1275		81	15	33	28		
YPK_TSS_277	+	1418441	140	YPK_1289	*ndk*	26		17	22		
YPK_TSS_278	+	1418451	130	YPK_1289	*ndk*	61					
YPK_TSS_279	+	1420978	382	YPK_1292	*yfgA*		14				
YPK_TSS_280	-	1431753	35	YPK_1301	*xseA*	3	3				
YPK_TSS_281	+	1431855	33	YPK_1302	*guaB*			12		11	
YPK_TSS_282	+	1450270	136	YPK_1320		10	26		19		
YPK_TSS_283	-	1452267	24	YPK_1322		12	12	21	28		
YPK_TSS_284	+	1452377	97	YPK_1323				22			16
YPK_TSS_285	-	1456855	28	YPK_1326			250	13		94	30
YPK_TSS_286	-	1456928	101	YPK_1326		17	10	19			
YPK_TSS_287	-	1483578	40	YPK_1344	*ppk*	58	35	37	87	32	26
YPK_TSS_288	-	1490671	33	YPK_1349	*speG*	21		59			
YPK_TSS_289	+	1493057	40	YPK_1352	*upp*	371		162			
YPK_TSS_290	+	1495368	27	YPK_1354		47	40	22		15	
YPK_TSS_291	-	1498427	75	YPK_1356		28	34	46	42	17	12
YPK_TSS_292	-	1502696	-16	YPK_1361	*gcvR*	23	10	21	13	10	
YPK_TSS_293	+	1502790	24	YPK_1362	*dapA*	12		17			
YPK_TSS_294	+	1505767	25	YPK_1366		48		55			
YPK_TSS_295	-	1512087	74	YPK_1373		12		10			
YPK_TSS_296	+	1512924	33	YPK_1375	*afuA, fbpA*		37	155			
YPK_TSS_297	+	1517424	26	YPK_1378	*ydeN*			16			
YPK_TSS_298	+	1527922	131	YPK_1385	*napF*		70				
YPK_TSS_299	-	1542213	63	YPK_1397	*ygiW*		53			10	
YPK_TSS_300	-	1545996	40	YPK_1401		23		10			
YPK_TSS_301	+	1547476	45	YPK_1404		130		89			
YPK_TSS_302	+	1550433	184	YPK_1407	*nanT*	16		20			
YPK_TSS_303	+	1552414	68	YPK_1408	*cysP*					58	
YPK_TSS_304	-	1576444	233	YPK_1426	*crr*	21	13		15		
YPK_TSS_305	-	1576599	388	YPK_1426	*crr*	34	30	46	10		12
YPK_TSS_306	-	1578327	34	YPK_1428	*ptsH*		35			10	
YPK_TSS_307	-	1578366	73	YPK_1428	*ptsH*	14		25			
YPK_TSS_308	-	1579795	35	YPK_1429	*cysK*	60	25	430		174	14
YPK_TSS_309	-	1580709	58	YPK_1430	*cysZ*	21	27	21		11	
YPK_TSS_310	+	1580853	47	YPK_1431	*zipA*	63	82	37	40	27	10
YPK_TSS_311	-	1587536	58	YPK_1437	*gltX*	5	12	42			
YPK_TSS_312	-	1587547	69	YPK_1437	*gltX*	12					
YPK_TSS_313	-	1590354	33	YPK_1438	*nupC1*			30			
YPK_TSS_314	-	1590396	75	YPK_1438	*nupC1*	41			0	11	
YPK_TSS_315	+	1590731	41	YPK_1439	*mntH*				11		
YPK_TSS_316	-	1594708	27	YPK_1442					13		10
YPK_TSS_317	+	1595405	36	YPK_1444	*glk*	11					
YPK_TSS_318	+	1597941	62	YPK_1446		19	15	68	14		14

tss id	strand	TSS position (+ strand)	Distance to start codon [nt]	Gene ID	name	Reads YPIII 25°C exp	Reads YPIII 25°C stat	Reads YPIII 37°C exp	Reads YPIII 37°C stat	Reads YP89 25°C stat	Reads YP89 37°C stat
YPK_TSS_319	-	1615783	53	YPK_1463	*sfuA*	78	35				
YPK_TSS_320	+	1616031	28	YPK_1464	*mltB*	13				10	
YPK_TSS_321	+	1658611	39	YPK_1496	*ccmA*			10			
YPK_TSS_322	-	1668015	53	YPK_1506	*fadL*	236					
YPK_TSS_323	-	1668060	98	YPK_1506	*fadL*	20	73	158	103		
YPK_TSS_324	+	1668893	66	YPK_1508	*fadI*		14	45	26		
YPK_TSS_325	+	1672877	172	YPK_1510					13		
YPK_TSS_326	+	1674736	86	YPK_1513		10		14	16		
YPK_TSS_327	+	1674783	39	YPK_1513		10			13	16	10
YPK_TSS_328	+	1679156	103	YPK_1518		15		10			
YPK_TSS_329	-	1681810	26	YPK_1519	*mnmC*	15		11			
YPK_TSS_330	+	1681917	39	YPK_1520	*fabB*	60	12	16		15	
YPK_TSS_331	+	1689381	43	YPK_1527	*pdxB*	17		26			
YPK_TSS_332	+	1693502	160	YPK_1531	*accD*	27	14	25			
YPK_TSS_333	+	1700376	357	YPK_1538	*hisJ*		18	22	14		
YPK_TSS_334	-	1704858	5	YPK_1542			11		13		
YPK_TSS_335	-	1704914	61	YPK_1542			28	13	40	21	
YPK_TSS_336	-	1709719	26	YPK_1548	*ulaC*	20		54			
YPK_TSS_337	-	1715078	194	YPK_1551	*ackA*	13					
YPK_TSS_338	+	1716588	141	YPK_1554		12		19			
YPK_TSS_339	+	1722957	78	YPK_1559	*rovM*					61	
YPK_TSS_340	+	1724341	304	YPK_1560	*nuoA*	32	74	31	19		
YPK_TSS_341	+	1724462	183	YPK_1560	*nuoA*		12				
YPK_TSS_342	+	1724511	134	YPK_1560	*nuoA*	73	22	54		15	
YPK_TSS_343	+	1746072	33	YPK_1578		17	8	13			
YPK_TSS_344	+	1753376	155	YPK_1585	*elaB*		29	0			
YPK_TSS_345	+	1753507	24	YPK_1585	*elaB*					95	
YPK_TSS_346	+	1757051	155	YPK_1589	*menD*	25	12	48	21		
YPK_TSS_347	-	1770719	334	YPK_1600	*glnH*					65	18
YPK_TSS_348	-	1772945	41	YPK_1602	*dps*		71		34	38	
YPK_TSS_349	+	1775722	43	YPK_1606	*ompX/ailD*	470	11	162		105	
YPK_TSS_350	-	1787208	38	YPK_1615	*dmlR*				17		
YPK_TSS_351	+	1803647	18	YPK_1624	*trp14A*	11	25		13	33	
YPK_TSS_352	+	1824266	232	YPK_1644	*cas-1*		52		33		
YPK_TSS_353	+	1837651	25	YPK_1655	*ypsR*		12		12		
YPK_TSS_354	-	1839078	28	YPK_1656	*ypsI*	37					
YPK_TSS_355	-	1842317	51	YPK_1658		10			19		
YPK_TSS_356	-	1842974	119	YPK_1659			13			10	
YPK_TSS_357	-	1850728	174	YPK_1664	*yceE*	10					
YPK_TSS_358	-	1852323	145	YPK_1665	*htrB*		11				
YPK_TSS_359	-	1859025	72	YPK_1673	*bssS*	79	430	91	126	80	16
YPK_TSS_360	-	1861127	64	YPK_1675	*pyrC*	20		22			
YPK_TSS_361	-	1865808	315	YPK_1677	*rne*		19		11		12
YPK_TSS_362	-	1865858	365	YPK_1677	*rne*	27	38	28	19	15	
YPK_TSS_363	+	1866068	0	YPK_1678	*rluC*	13					
YPK_TSS_364	+	1868496	88	YPK_1681		234	18	81		15	
YPK_TSS_365	+	1868846	275	YPK_1682	*rpmF*	572	17	157		51	
YPK_TSS_366	+	1872117	177	YPK_1686	*fabG*	19		38		53	
YPK_TSS_367	+	1873143	39	YPK_1687	*acpP*	1002	495	635	234	209	
YPK_TSS_368	+	1879900	116	YPK_1694	*ptsG*	11		18			
YPK_TSS_369	+	1882788	33	YPK_1696		17		13			
YPK_TSS_370	-	1894917	215	YPK_1706	*mfd*				19	10	
YPK_TSS_371	+	1894938	34	YPK_1707	*lolC*	10					
YPK_TSS_372	-	1902898	26	YPK_1713		12					
YPK_TSS_373	-	1905177	90	YPK_1715	*phoP*		33	46	12		
YPK_TSS_374	+	1910635	91	YPK_1723	*icdA*	25	44	44	39		
YPK_TSS_375	+	1910682	44	YPK_1723	*icdA*	410	327	522	197	246	20
YPK_TSS_376	-	1913718	31	YPK_1725		30	82	24			
YPK_TSS_377	+	1917274	26	YPK_1728					14		
YPK_TSS_378	-	1917285	121	YPK_1727				14			
YPK_TSS_379	-	1918050	23	YPK_1729		10	35	11	28		
YPK_TSS_380	-	1920103	34	YPK_1731					157		
YPK_TSS_381	-	1920166	97	YPK_1731					64		
YPK_TSS_382	-	1920222	153	YPK_1731		74	117	17	34	35	66
YPK_TSS_383	-	1921302	31	YPK_1732				10	16		
YPK_TSS_384	-	1924445	49	YPK_1738		435	163	386	170	213	101
YPK_TSS_385	-	1924462	66	YPK_1738						17	
YPK_TSS_386	-	1927841	85	YPK_1739	*lacZ*		14	12	12		
YPK_TSS_387	+	1928117	180	YPK_1740	*cspC-1*	411	126	28	12	26	
YPK_TSS_388	+	1928700	24	YPK_1741		21	11	34			
YPK_TSS_389	+	1936535	398	YPK_1745	*flhD*	28	91	10	28		
YPK_TSS_390	+	1954861	76	YPK_1760	*cwlA, xlyA, xlyB*			14			
YPK_TSS_391	-	1962208	23	YPK_1765			63		50	35	22
YPK_TSS_392	+	1962709	25	YPK_1767		44	15	62		21	
YPK_TSS_393	+	1964765	21	YPK_1769		28	52		18		
YPK_TSS_394	+	1978074	47	YPK_1782	*proQ*	32	47	217	14		
YPK_TSS_395	+	1983462	144	YPK_1787	*ecpD*		49		18		
YPK_TSS_396	+	1983473	133	YPK_1787	*ecpD*					94	
YPK_TSS_397	-	1990496	36	YPK_1791	*yebQ*					18	
YPK_TSS_398	-	1990628	168	YPK_1791	*yebQ*		28		11	40	12
YPK_TSS_399	+	1992113	67	YPK_1793	*kdgR*	27	15	10			
YPK_TSS_400	-	1995875	81	YPK_1795	*gltP*	19					
YPK_TSS_401	-	1995927	133	YPK_1795	*gltP*		40				
YPK_TSS_402	-	2011171	28	YPK_1811	*yniA*	11	19	15	10		
YPK_TSS_403	-	2011185	42	YPK_1811	*yniA*					65	
YPK_TSS_404	+	2014966	322	YPK_1816	*mltE*	10	17		44		
YPK_TSS_405	+	2017046	28	YPK_1818		151	172	162	228	22	
YPK_TSS_406	+	2018521	166	YPK_1820	*thrS*	18		10		12	
YPK_TSS_407	+	2020438	382	YPK_1821	*infC*	270	182	265	159	67	30
YPK_TSS_408	+	2025578	168	YPK_1826	*ihfA*	204	119	262	131	204	10
YPK_TSS_409	+	2029729	96	YPK_1831	*pmrH*	13					

tss id	strand	TSS position (+ strand)	Distance to start codon [nt]	Gene ID	name	Reads YPIII 25°C exp	Reads YPIII 25°C stat	Reads YPIII 37°C exp	Reads YPIII 37°C stat	Reads YP89 25°C stat	Reads YP89 37°C stat
YPK_TSS_410	+	2037308	208	YPK_1838	*nlpC*	26	92	12	199	29	20
YPK_TSS_411	-	2041902	51	YPK_1841	*aroH*	14					
YPK_TSS_412	+	2051995	122	YPK_1847	*sufA*	29					
YPK_TSS_413	+	2058168	76	YPK_1853		54	20	38	16		
YPK_TSS_414	-	2059942	38	YPK_1854	*lpp*	5094	3494	6831	954	2084	356
YPK_TSS_415	-	2061903	266	YPK_1855	*pykF*	20					
YPK_TSS_416	-	2064343	76	YPK_1856			10				
YPK_TSS_417	+	2064472	44	YPK_1857	*ribE*					15	
YPK_TSS_418	-	2066443	69	YPK_1858	*cfa*			38			
YPK_TSS_419	-	2066687	313	YPK_1858	*cfa*		12		17	14	18
YPK_TSS_420	-	2068239	183	YPK_1859		15					
YPK_TSS_421	-	2071600	89	YPK_1863	*sodB*			20	32	36	28
YPK_TSS_422	-	2072881	143	YPK_1864						10	
YPK_TSS_423	+	2072999	179	YPK_1866	*grxD*	60	55	42	42	66	14
YPK_TSS_424	+	2073098	80	YPK_1866	*grxD*	20		24			
YPK_TSS_425	-	2074508	-9	YPK_1868	*rnt*	17	12	10		25	
YPK_TSS_426	-	2075057	54	YPK_1869	*gloA*	15		12			
YPK_TSS_427	+	2075217	59	YPK_1870	*sepC*		10			14	12
YPK_TSS_428	+	2082041	343	YPK_1876	*rovA*	66	32				
YPK_TSS_429	+	2082307	77	YPK_1876	*rovA*	47	81				
YPK_TSS_430	+	2082340	44	YPK_1876	*rovA*	65	73	18	13	7	
YPK_TSS_431	-	2083622	196	YPK_1877	*slyB*	14	10	37	13		
YPK_TSS_432	+	2085255	233	YPK_1880	*pdxH*		119		64		
YPK_TSS_433	+	2086262	130	YPK_1881	*tyrS*	15					
YPK_TSS_434	+	2087626	195	YPK_1882	*pdxY*	37	160	57	20	205	38
YPK_TSS_435	-	2089381	35	YPK_1883	*gst*		31	16		18	
YPK_TSS_436	-	2090779	89	YPK_1885			90		10	10	
YPK_TSS_437	-	2092548	67	YPK_1886	*tppB*	25		16			
YPK_TSS_438	-	2100081	26	YPK_1892	*sapA*	12		11			
YPK_TSS_439	+	2101776	110	YPK_1894	*pspA*	16	11	20			
YPK_TSS_440	-	2107075	37	YPK_1901		22	47	69	167	31	28
YPK_TSS_441	+	2107336	39	YPK_1902	*tyrR*	25	14	28			
YPK_TSS_442	-	2109667	31	YPK_1903	*tpx*					283	
YPK_TSS_443	-	2109674	38	YPK_1903	*tpx*	127	16	158	26	116	
YPK_TSS_444	+	2111797	166	YPK_1906	*mppA*				12		
YPK_TSS_445	-	2118580	34	YPK_1912				10			
YPK_TSS_446	-	2126114	22	YPK_1918	*ldhA*	28	30				
YPK_TSS_447	-	2126157	65	YPK_1918	*ldhA*		16	26	17		
YPK_TSS_448	-	2133162	49	YPK_1924	*acpD*	18		15			
YPK_TSS_449	-	2140030	103	YPK_1929			11		13		
YPK_TSS_450	-	2149989	24	YPK_1937	*rstA*	25	20	22	27	14	
YPK_TSS_451	+	2150164	98	YPK_1938			15		21		
YPK_TSS_452	-	2153383	67	YPK_1940		32		26			
YPK_TSS_453	+	2153659	187	YPK_1941	*pntA*	22	10			12	
YPK_TSS_454	-	2158815	25	YPK_1944	*fnr*	75	26	56	27	64	26
YPK_TSS_455	-	2159420	39	YPK_1945	*ogt*	36	16	68	110	21	
YPK_TSS_456	+	2164128	28	YPK_1948		19					
YPK_TSS_457	-	2173190	56	YPK_1954		25					
YPK_TSS_458	+	2178580	114	YPK_1960					31		
YPK_TSS_459	+	2188538	38	YPK_1971					10		
YPK_TSS_460	+	2194757	2	YPK_1975			40	20	21		
YPK_TSS_461	+	2198222	59	YPK_1978		22	522	10	127	104	28
YPK_TSS_462	-	2202232	66	YPK_1981	*mlc*				40		
YPK_TSS_463	-	2203286	27	YPK_1982	*ynfL*		34			13	
YPK_TSS_464	+	2203333	139	YPK_1983	*ynfM*		29				
YPK_TSS_465	+	2208976	110	YPK_1987		22	11	18			
YPK_TSS_466	-	2211633	37	YPK_1988		12	13				
YPK_TSS_467	+	2211763	88	YPK_1989		11	17	38	10		
YPK_TSS_468	+	2214670	48	YPK_1993	*add*	15		23			
YPK_TSS_469	-	2218227	59	YPK_1995		13	19	17		19	
YPK_TSS_470	-	2219367	139	YPK_1996	*araC*		28		10		
YPK_TSS_471	+	2233840	29	YPK_2006		33	19	12			
YPK_TSS_472	+	2244864	38	YPK_2016	*rnb*	27		22			
YPK_TSS_473	+	2247110	76	YPK_2017	*cstA-1*		28				
YPK_TSS_474	+	2252030	90	YPK_2022	*osmB*	11		18	12		
YPK_TSS_475	-	2253736	35	YPK_2024	*pyrF*	60	29	80	20	16	
YPK_TSS_476	-	2256103	25	YPK_2027		18	17				
YPK_TSS_477	-	2256135	57	YPK_2027					15		
YPK_TSS_478	-	2256231	153	YPK_2027			22				
YPK_TSS_479	-	2261167	215	YPK_2030	*acnA*				17		
YPK_TSS_480	-	2268360	35	YPK_2036	*sohB*	19	10	14		14	
YPK_TSS_481	+	2268445	52	YPK_2037				13			
YPK_TSS_482	+	2276341	159	YPK_2045	*trpC*	12	10		10		
YPK_TSS_483	+	2280262	139	YPK_2048			17		11	16	
YPK_TSS_484	-	2281525	28	YPK_2049	*ompW*			12			
YPK_TSS_485	+	2281949	34	YPK_2050	*yciC*	11		13			
YPK_TSS_486	-	2286775	21	YPK_2055	*tonB*	125					
YPK_TSS_487	-	2288239	26	YPK_2059			27	29			
YPK_TSS_488	-	2289121	149	YPK_2061	*ailB*		11				
YPK_TSS_489	+	2289989	29	YPK_2063	*cls*	10		16			
YPK_TSS_490	+	2291583	30	YPK_2064		31	10	28	20		
YPK_TSS_491	-	2298904	274	YPK_2070	*oppA*	16	25				
YPK_TSS_492	+	2300748	233	YPK_2072	*adhE*	134	4	27	9		
YPK_TSS_493	+	2300933	48	YPK_2072	*adhE*	197	22				
YPK_TSS_494	+	2305710	37	YPK_2074	*hns*	410	82	233	49	23	
YPK_TSS_495	-	2309281	23	YPK_2078					14		
YPK_TSS_496	+	2310507	85	YPK_2079		18	43	22	47	11	
YPK_TSS_497	+	2314519	29	YPK_2085	*xthA*	13		22			
YPK_TSS_498	+	2320099	26	YPK_2091	*sppA*	32		28			
YPK_TSS_499	-	2324702	42	YPK_2095	*msrB*	23	22	55			
YPK_TSS_500	+	2324762	246	YPK_2096	*gapA*	28	88	12	14		30
YPK_TSS_501	+	2324833	175	YPK_2096	*gapA*	21	16	35	14		

tss id	strand	TSS position (+ strand)	Distance to start codon [nt]	Gene ID	name	Reads YPIII 25°C exp	Reads YPIII 25°C stat	Reads YPIII 37°C exp	Reads YPIII 37°C stat	Reads YP89 25°C stat	Reads YP89 37°C stat
YPK_TSS_502	+	2324852	156	YPK_2096	*gapA*	61					
YPK_TSS_503	+	2324940	68	YPK_2096	*gapA*	10		12			
YPK_TSS_504	+	2324972	36	YPK_2096	*gapA*	277	10	81		21	
YPK_TSS_505	+	2326280	47	YPK_2097		40	42	38	36		
YPK_TSS_506	-	2328079	34	YPK_2098	*mipA, yiaT*	70	38	442	36	35	
YPK_TSS_507	-	2328115	70	YPK_2098	*mipA, yiaT*	11		53			
YPK_TSS_508	-	2328197	152	YPK_2098	*mipA, yiaT*	16		49	17		
YPK_TSS_509	+	2331902	32	YPK_2103						11	
YPK_TSS_510	+	2338270	46	YPK_2108			19				
YPK_TSS_511	-	2340828	40	YPK_2109	*fadR*	27	15	13	16		
YPK_TSS_512	+	2342812	30	YPK_2111	*dsbB*	22	21		11		
YPK_TSS_513	-	2344171	26	YPK_2113		28					
YPK_TSS_514	-	2351436	192	YPK_2120			14	11			
YPK_TSS_515	+	2351896	69	YPK_2121	*minC*	16	13		13		
YPK_TSS_516	-	2357030	63	YPK_2125	*fadD*		22		13		
YPK_TSS_517	-	2358243	28	YPK_2126			41				
YPK_TSS_518	+	2365849	27	YPK_2135	*hexR*	22	16	15	18		
YPK_TSS_519	-	2376124	225	YPK_2144	*ruvA*	16		14			
YPK_TSS_520	-	2376910	183	YPK_2145	*ruvC*	25			11		
YPK_TSS_521	+	2381803	31	YPK_2150		31	26	24	18	22	
YPK_TSS_522	-	2385201	54	YPK_2153	*cutC*		41				
YPK_TSS_523	-	2385328	181	YPK_2153	*cutC*	11	27				
YPK_TSS_524	-	2385992	38	YPK_2154		43		52			
YPK_TSS_525	+	2386273	298	YPK_2155	*argS*	6					6
YPK_TSS_526	+	2386543	28	YPK_2155	*argS*			12			
YPK_TSS_527	-	2399435	33	YPK_2161	*rimJ*					26	
YPK_TSS_528	-	2420142	-8	YPK_2180	*hemA*	22	10	16			
YPK_TSS_529	+	2421749	332	YPK_2183		34	12	46			
YPK_TSS_530	-	2423780	90	YPK_2185					16		
YPK_TSS_531	+	2433476	26	YPK_2196			15	16			
YPK_TSS_532	+	2438097	84	YPK_2200			215	310	12794	470	7264
YPK_TSS_533	-	2459937	63	YPK_2219			42		14		
YPK_TSS_534	+	2462252	111	YPK_2222	*hutI*			32		12	
YPK_TSS_535	-	2481027	190	YPK_2236			47			24	
YPK_TSS_536	-	2498349	293	YPK_2251			17				
YPK_TSS_537	-	2503698	161	YPK_2254	*glsA*		12		29		
YPK_TSS_538	-	2511421	29	YPK_2259			4		10		
YPK_TSS_539	-	2543391	0	YPK_2295		85	152	55	78	118	24
YPK_TSS_540	-	2555798	54	YPK_2310					19		
YPK_TSS_541	-	2555804	60	YPK_2310		12	15	14			
YPK_TSS_542	-	2588099	35	YPK_2354	*pgsA*	51	117	41	83	49	22
YPK_TSS_543	-	2590652	48	YPK_2356	*uvrY*	3	9				
YPK_TSS_544	+	2591219	48	YPK_2357		51	23	25		14	
YPK_TSS_545	-	2601452	74	YPK_2366		9					
YPK_TSS_546	-	2603440	0	YPK_2368		10		14			
YPK_TSS_547	+	2603743	42	YPK_2369	*putA*	14		14			
YPK_TSS_548	+	2608296	-2	YPK_2371					13		
YPK_TSS_549	-	2612627	8	YPK_2377	*YedO*	15	13	14		10	
YPK_TSS_550	-	2614375	28	YPK_2380	*fliA*	21					
YPK_TSS_551	-	2614547	200	YPK_2380	*fliA*	11					
YPK_TSS_552	-	2615868	65	YPK_2381	*fliC*	569					
YPK_TSS_553	+	2616051	49	YPK_2382	*fliD*	16					
YPK_TSS_554	+	2618558	25	YPK_2385		11					
YPK_TSS_555	+	2622807	120	YPK_2387			12		13		
YPK_TSS_556	-	2624474	84	YPK_2389		44	67	91	58	20	26
YPK_TSS_557	-	2625255	118	YPK_2390	*fliE*	28					
YPK_TSS_558	+	2625360	130	YPK_2391	*fliF*	59					
YPK_TSS_559	+	2632332	124	YPK_2398	*fliL*	36					
YPK_TSS_560	+	2637109	50	YPK_2405			14		18		
YPK_TSS_561	+	2646021	187	YPK_2414				14			
YPK_TSS_562	-	2650117	96	YPK_2416	*flgK*	20					
YPK_TSS_563	-	2657845	27	YPK_2425	*flgB*	176					
YPK_TSS_564	+	2657952	39	YPK_2426	*flgA*	33					
YPK_TSS_565	-	2663030	229	YPK_2429	*invA*		41				
YPK_TSS_566	-	2666024	66	YPK_2431	*flhA*	15					
YPK_TSS_567	+	2667599	51	YPK_2433					10	20	10
YPK_TSS_568	-	2670699	31	YPK_2437				34			
YPK_TSS_569	-	2670863	195	YPK_2437		15	15		10		
YPK_TSS_570	-	2671591	35	YPK_2438	*ftnA*				18		
YPK_TSS_571	-	2671600	44	YPK_2438	*ftnA*		11	27		49	
YPK_TSS_572	+	2671925	32	YPK_2439	*holE*			22			
YPK_TSS_573	+	2673482	37	YPK_2441		38	1157	59	41	275	10
YPK_TSS_574	-	2676024	54	YPK_2442	*ptrB*	10		16			
YPK_TSS_575	-	2677096	-9	YPK_2444			93		17	14	10
YPK_TSS_576	-	2677502	37	YPK_2445				13			
YPK_TSS_577	-	2679004	63	YPK_2446	*dbpA*	21		14			
YPK_TSS_578	+	2682174	182	YPK_2450			23			16	
YPK_TSS_579	+	2683152	531	YPK_2451	*sdaA*	10					
YPK_TSS_580	+	2695052	55	YPK_2462	*hpcR*	13	21	15	21	20	
YPK_TSS_581	-	2697467	247	YPK_2463	*yoaE*	42	36	15			
YPK_TSS_582	+	2697752	179	YPK_2464	*manX*	100	68	104	26		
YPK_TSS_583	+	2697845	86	YPK_2464	*manX*		27				
YPK_TSS_584	+	2701574	201	YPK_2468	*yebN*	18		11			
YPK_TSS_585	-	2704854	43	YPK_2469	*fcuA*	17					
YPK_TSS_586	+	2707432	26	YPK_2471			14		10		
YPK_TSS_587	-	2708848	51	YPK_2472	*rrmA*	13		11			
YPK_TSS_588	-	2710429	26	YPK_2475		1323	1078	1432	799	161	22
YPK_TSS_589	-	2713749	67	YPK_2477	*aroP*	21		19			
YPK_TSS_590	-	2715139	29	YPK_2480		13					
YPK_TSS_591	-	2716284	28	YPK_2482			13		13		
YPK_TSS_592	-	2716653	73	YPK_2483		25	3101	72	267	71	127
YPK_TSS_593	-	2717732	98	YPK_2486			13		13		

tss id	strand	TSS position (+ strand)	Distance to start codon [nt]	Gene ID	name	Reads YPIII 25°C exp	Reads YPIII 25°C stat	Reads YPIII 37°C exp	Reads YPIII 37°C stat	Reads YP89 25°C stat	Reads YP89 37°C stat
YPK_TSS_594	-	2717769	135	YPK_2486						16	
YPK_TSS_595	+	2720952	56	YPK_2489				26			
YPK_TSS_596	+	2721503	179	YPK_2490					20		
YPK_TSS_597	-	2724022	106	YPK_2491	*thuR*		22	16	21		
YPK_TSS_598	+	2732576	94	YPK_2499	*uhpA*					38	
YPK_TSS_599	+	2732646	24	YPK_2499	*uhpA*	8	4	3			
YPK_TSS_600	+	2735921	163	YPK_2502			17				
YPK_TSS_601	-	2742930	120	YPK_2506	*lldD*			14	21		
YPK_TSS_602	-	2746161	115	YPK_2510			24		23		
YPK_TSS_603	-	2748368	121	YPK_2512			21				
YPK_TSS_604	-	2753026	51	YPK_2514					11		
YPK_TSS_605	-	2753065	90	YPK_2514				13			
YPK_TSS_606	-	2753142	167	YPK_2514		11		27			
YPK_TSS_607	-	2760347	152	YPK_2518		21					
YPK_TSS_608	-	2761597	57	YPK_2519		6	4	4	7	5	
YPK_TSS_609	+	2761700	126	YPK_2520					10		
YPK_TSS_610	-	2776294	65	YPK_2535	*gnd*	146	41	562	24	18	
YPK_TSS_611	+	2794386	224	YPK_2549						23	
YPK_TSS_612	+	2794427	183	YPK_2549			16	12			
YPK_TSS_613	-	2799769	58	YPK_2552	*udk*	13		10			
YPK_TSS_614	-	2801108	40	YPK_2553		30		22			
YPK_TSS_615	+	2801297	36	YPK_2554	*metG*	14	19	31			
YPK_TSS_616	-	2804445	126	YPK_2555						49	10
YPK_TSS_617	+	2810361	23	YPK_2561	*cdd*	26		12			
YPK_TSS_618	+	2811586	38	YPK_2562	*sfcA*	14	24	11			
YPK_TSS_619	-	2818797	240	YPK_2566	*mglB*	10	29	20	49		
YPK_TSS_620	-	2818828	271	YPK_2566	*mglB*		17	16	11		
YPK_TSS_621	-	2821253	65	YPK_2568	*folE*	43	21	34			
YPK_TSS_622	+	2824549	413	YPK_2572	*frmB, fghA*		146	36	86		
YPK_TSS_623	-	2837146	62	YPK_2581	*ybiT*	50		10		10	
YPK_TSS_624	+	2876488	25	YPK_2621		16			15		
YPK_TSS_625	-	2877431	76	YPK_2622			12				
YPK_TSS_626	+	2877555	116	YPK_2623			13		22		
YPK_TSS_627	+	2877647	24	YPK_2623		20	31	18	26	34	
YPK_TSS_628	+	2878497	33	YPK_2624	*mgsA*	17		21	30	16	
YPK_TSS_629	+	2881516	263	YPK_2627					30		
YPK_TSS_630	-	2884723	69	YPK_2628	*tfoX*				11		
YPK_TSS_631	+	2885685	62	YPK_2630	*ompA*	154	51	134		43	
YPK_TSS_632	-	2888108	28	YPK_2632		44	34	47	15	15	
YPK_TSS_633	+	2888260	160	YPK_2633		37		11			
YPK_TSS_634	+	2891221	108	YPK_2636	*fabF2*	3	7	6			
YPK_TSS_635	-	2900798	28	YPK_2641	*rlmL*	10					
YPK_TSS_636	-	2901152	382	YPK_2641	*rlmL*			5			
YPK_TSS_637	-	2903797	45	YPK_2644	*pyrD*		11	37	140		58
YPK_TSS_638	-	2904109	357	YPK_2644	*pyrD*				11		
YPK_TSS_639	-	2907108	105	YPK_2645	*pepN*	23	22	41		10	
YPK_TSS_640	+	2907610	75	YPK_2647	*pncB*				11	13	
YPK_TSS_641	+	2909196	184	YPK_2648	*asnC*	44	20	26		12	
YPK_TSS_642	+	2910984	94	YPK_2649	*ompF*	1781	668	94	57	80	
YPK_TSS_643	+	2912378	39	YPK_2650	*aspC*	11	29	49		10	
YPK_TSS_644	-	2915181	83	YPK_2653		4		4			
YPK_TSS_645	-	2924334	423	YPK_2657	*mukF*			11			
YPK_TSS_646	-	2927707	35	YPK_2661		12		12			
YPK_TSS_647	-	2928902	473	YPK_2662	*cspB-2*	5	5		7	4	
YPK_TSS_648	+	2929053	95	YPK_2663			27		22		
YPK_TSS_649	-	2933323	27	YPK_2665	*msbA*			15			
YPK_TSS_650	-	2935694	71	YPK_2666	*comEC*		24				
YPK_TSS_651	-	2938332	158	YPK_2668	*rpsA*	232	15	134			
YPK_TSS_652	-	2938523	349	YPK_2668	*rpsA*	75	22	18			
YPK_TSS_653	-	2939099	59	YPK_2669	*cmk*	54	21	10			
YPK_TSS_654	-	2939174	134	YPK_2669	*cmk*		23			10	
YPK_TSS_655	-	2941942	45	YPK_2671	*serC*	49	17	32	17	21	
YPK_TSS_656	+	2949150	44	YPK_2676	*focA*		18				
YPK_TSS_657	+	2949162	32	YPK_2676	*focA*	46		18			
YPK_TSS_658	+	2953736	369	YPK_2679	*pflA*				35		
YPK_TSS_659	-	2956236	32	YPK_2680				11			
YPK_TSS_660	-	2957949	214	YPK_2681	*serS*	27	14	13		16	
YPK_TSS_661	-	2965016	338	YPK_2686	*lrp*	10					
YPK_TSS_662	+	2965416	30	YPK_2687	*trxB*	11					
YPK_TSS_663	+	2966680	187	YPK_2688	*cydD*	11	28	12	12		
YPK_TSS_664	+	2971419	36	YPK_2691	*infA*	134		184			
YPK_TSS_665	-	2974528	181	YPK_2692	*clpA*	19		19		31	
YPK_TSS_666	-	2974736	43	YPK_2693	*clpS*			24		2	
YPK_TSS_667	-	2974770	77	YPK_2693	*clpS*	17	14			15	
YPK_TSS_668	+	2974856	198	YPK_2694	*cspD*						12
YPK_TSS_669	+	2974962	92	YPK_2694	*cspD*		140	12	27		
YPK_TSS_670	+	2981822	178	YPK_2700		14	11				
YPK_TSS_671	+	2986000	28	YPK_2703	*poxB*	12	39	41	12	26	10
YPK_TSS_672	+	2988120	36	YPK_2705	*ltaA*		18			16	20
YPK_TSS_673	+	2988167	-11	YPK_2705	*ltaA*			19	21		
YPK_TSS_674	-	3013292	244	YPK_2732			12		10		
YPK_TSS_675	+	3013415	96	YPK_2733	*grxA*	14					
YPK_TSS_676	+	3017854	29	YPK_2737	*deoC*	22					
YPK_TSS_677	+	3018269	515	YPK_2738	*deoR*		24				
YPK_TSS_678	+	3018753	31	YPK_2738	*deoR*			3	7		
YPK_TSS_679	+	3020393	242	YPK_2739	*sdaC*	20					
YPK_TSS_680	-	3023746	131	YPK_2740	*dacC*	15	14	34	14	15	
YPK_TSS_681	-	3035174	5	YPK_2751	*fhuD, fepB, fecB*	61					
YPK_TSS_682	-	3037053	111	YPK_2752	*lysP*					28	
YPK_TSS_683	-	3038128	56	YPK_2754			23		11		
YPK_TSS_684	-	3038153	81	YPK_2754			11				

tss id	strand	TSS position (+ strand)	Distance to start codon [nt]	Gene ID	name	Reads YPIII 25°C exp	Reads YPIII 25°C stat	Reads YPIII 37°C exp	Reads YPIII 37°C stat	Reads YP89 25°C stat	Reads YP89 37°C stat
YPK_TSS_685	+	3039963	19	YPK_2756	*nfo*	36	11	46			
YPK_TSS_686	-	3046642	63	YPK_2761	*psaE*		248		56		
YPK_TSS_687	-	3046657	78	YPK_2761	*psaE*		53				
YPK_TSS_688	-	3059342	63	YPK_2771	*gabD-2*		11				
YPK_TSS_689	+	3064574	34	YPK_2777		18					
YPK_TSS_690	-	3066750	237	YPK_2778	*uxuA*				23		
YPK_TSS_691	-	3069494	71	YPK_2780	*uxuR*	11					
YPK_TSS_692	-	3069940	25	YPK_2781		94	10				
YPK_TSS_693	+	3071221	52	YPK_2783		12					
YPK_TSS_694	+	3072179	237	YPK_2784	*spr*	25	15	10			
YPK_TSS_695	+	3072359	57	YPK_2784	*spr*	42	150	58	21		
YPK_TSS_696	+	3075206	42	YPK_2786	*yejA*	11	10	27	18	11	
YPK_TSS_697	-	3084504	298	YPK_2793	*rsuA*		12				10
YPK_TSS_698	+	3086567	92	YPK_2795	*rplY*	56	21	36			
YPK_TSS_699	-	3088055	20	YPK_2796				5			
YPK_TSS_700	+	3088185	28	YPK_2797		10	13	10			
YPK_TSS_701	+	3093417	51	YPK_2804			16		20		
YPK_TSS_702	-	3112918	30	YPK_2826				21	12		
YPK_TSS_703	+	3113852	0	YPK_2829					20	12	
YPK_TSS_704	+	3114756	24	YPK_2830	*msgA*			10			
YPK_TSS_705	+	3121455	178	YPK_2836	*ampH*					21	
YPK_TSS_706	+	3121526	107	YPK_2836	*ampH*		13				
YPK_TSS_707	+	3121607	26	YPK_2836	*ampH*	16					
YPK_TSS_708	+	3123978	57	YPK_2838				10			
YPK_TSS_709	-	3125863	68	YPK_2839	*ompC-1*			438			
YPK_TSS_710	+	3130486	287	YPK_2843	*rcsB*	29	44	33	54	36	
YPK_TSS_711	+	3130569	204	YPK_2843	*rcsB*	262	85	294	61	137	
YPK_TSS_712	-	3134388	21	YPK_2844	*rcsC*		12				
YPK_TSS_713	-	3137287	39	YPK_2846	*gyrA*	106	62	87	41	16	10
YPK_TSS_714	+	3137520	28	YPK_2847	*ubiG*	16		12			
YPK_TSS_715	+	3138625	145	YPK_2848	*nrdA*	33		18			
YPK_TSS_716	-	3144428	22	YPK_2852		21	12	27			
YPK_TSS_717	-	3147092	60	YPK_2854						42	
YPK_TSS_718	+	3147272	121	YPK_2855	*katA*		13		10	10	
YPK_TSS_719	+	3153864	28	YPK_2859		22	18				
YPK_TSS_720	+	3163187	56	YPK_2866	*ynjE, sseA*	13	11	18	13		
YPK_TSS_721	-	3166569	28	YPK_2868						12	
YPK_TSS_722	-	3173373	81	YPK_2874		43	13	39	14		
YPK_TSS_723	-	3177761	119	YPK_2879			440		12	133	10
YPK_TSS_724	-	3177812	170	YPK_2879						15	
YPK_TSS_725	+	3179214	29	YPK_2881		11	17	20			
YPK_TSS_726	-	3183170	7	YPK_2885	*pbpG*	36		48			
YPK_TSS_727	-	3192594	129	YPK_2898	*rhlE*	195	64	59	35	17	93
YPK_TSS_728	-	3217906	57	YPK_2918		74	71	58	30	25	
YPK_TSS_729	-	3220708	217	YPK_2922	*moaA*		10				
YPK_TSS_730	-	3224697	68	YPK_2926	*uvrB*	19		11			
YPK_TSS_731	-	3230338	28	YPK_2931	*bioB*		11				
YPK_TSS_732	-	3232960	81	YPK_2933		26	55	55	20	14	0
YPK_TSS_733	-	3232981	102	YPK_2933			10				
YPK_TSS_734	-	3236659	65	YPK_2937	*modA*	14					
YPK_TSS_735	-	3237013	32	YPK_2938		31	14	39		29	
YPK_TSS_736	-	3237083	102	YPK_2938		12	10	36			
YPK_TSS_737	+	3245563	89	YPK_2947	*psiF*		28				
YPK_TSS_738	-	3248335	15	YPK_2949	*aroG*				18	11	
YPK_TSS_739	-	3248354	34	YPK_2949	*aroG*	8		15	5		
YPK_TSS_740	-	3254547	259	YPK_2955	*pal*	1215	203	1550	2236	292	3608
YPK_TSS_741	-	3255669	38	YPK_2956	*tolB*	30	22	49	41	1	10
YPK_TSS_742	-	3258582	25	YPK_2960		189	198	122	59	191	66
YPK_TSS_743	-	3258679	122	YPK_2960			41				
YPK_TSS_744	-	3258782	225	YPK_2960			14				
YPK_TSS_745	-	3259038	17	YPK_2961			40			37	
YPK_TSS_746	-	3268960	146	YPK_2968	*kgd*	262	430	717	33	239	20
YPK_TSS_747	-	3268985	171	YPK_2968	*kgd*		11	19			
YPK_TSS_748	-	3272596	163	YPK_2972	*sdhC*	176	237	396	115		14
YPK_TSS_749	+	3272755	388	YPK_2973	*gltA*	11	10	20	32		
YPK_TSS_750	+	3272831	312	YPK_2973	*gltA*	11		11			
YPK_TSS_751	+	3272880	263	YPK_2973	*gltA*	13		37		15	
YPK_TSS_752	-	3275143	34	YPK_2974	*GrpE*	166		88			
YPK_TSS_753	+	3277902	74	YPK_2977				26			
YPK_TSS_754	+	3277949	27	YPK_2977		27		10			
YPK_TSS_755	-	3279202	24	YPK_2979		30	23	36			
YPK_TSS_756	+	3279336	-9	YPK_2980	*smpB*	90	12	37		12	
YPK_TSS_757	+	3283569	-7	YPK_2988		16					
YPK_TSS_758	+	3283583	167	YPK_2989				10	12	5	4
YPK_TSS_759	+	3284402	52	YPK_2990	*fldA*			19			
YPK_TSS_760	+	3285221	127	YPK_2991	*fur*	31	71	12	31	17	
YPK_TSS_761	+	3285269	79	YPK_2991	*fur*	19					
YPK_TSS_762	-	3293065	33	YPK_2994	*glnS*	31		39			
YPK_TSS_763	-	3296126	135	YPK_2996	*nagE*	44	10	290			
YPK_TSS_764	+	3296255	135	YPK_2997	*nagB*	14		14			
YPK_TSS_765	+	3299476	195	YPK_3000	*nagD*	36	26	37	22	10	12
YPK_TSS_766	+	3306949	152	YPK_3006		4	8	5	8		
YPK_TSS_767	+	3307014	87	YPK_3006		20	16	23	22		
YPK_TSS_768	+	3309592	56	YPK_3009	*lnt*	56	163	185	21	210	22
YPK_TSS_769	+	3311778	198	YPK_3010	*ybeJ/gltI*		74		42		
YPK_TSS_770	+	3311800	176	YPK_3010	*ybeJ/gltI*		241	34			
YPK_TSS_771	-	3315849	27	YPK_3014			31	20			
YPK_TSS_772	+	3316012	72	YPK_3015	*leuS*	26		17			
YPK_TSS_773	+	3321111	99	YPK_3019		11		5			
YPK_TSS_774	+	3321237	294	YPK_3020			35	54	17	22	232
YPK_TSS_775	+	3326733	38	YPK_3024	*dacA*	33		45			
YPK_TSS_776	+	3328629	17	YPK_3026	*lipB*	97	29	44	16	24	

tss id	strand	TSS position (+ strand)	Distance to start codon [nt]	Gene ID	name	Reads YPIII 25°C exp	Reads YPIII 25°C stat	Reads YPIII 37°C exp	Reads YPIII 37°C stat	Reads YP89 25°C stat	Reads YP89 37°C stat
YPK_TSS_777	-	3331045	102	YPK_3028	*tatE*	10		16		18	
YPK_TSS_778	-	3332568	43	YPK_3031	*cspE*	19	170	200	42		
YPK_TSS_779	+	3334426	167	YPK_3034		10	55		37		
YPK_TSS_780	-	3336152	21	YPK_3035		54	107	83	143		
YPK_TSS_781	-	3349143	119	YPK_3046			26				
YPK_TSS_782	+	3353143	19	YPK_3051		19	10	19	31	10	10
YPK_TSS_783	-	3374802	16	YPK_3069	*rluF*	6	4	3			
YPK_TSS_784	+	3392923	125	YPK_3087		29	71	35	25	27	
YPK_TSS_785	-	3399098	269	YPK_3094			19				
YPK_TSS_786	-	3400482	92	YPK_3097		65	43	95	32	71	50
YPK_TSS_787	-	3400598	208	YPK_3097			97		24	16	
YPK_TSS_788	+	3402788	0	YPK_3102		21	13	24	13	16	12
YPK_TSS_789	+	3404146	-12	YPK_3104			26		22		
YPK_TSS_790	+	3406827	23	YPK_3108		11		13			
YPK_TSS_791	+	3439316	27	YPK_3146			14	12			
YPK_TSS_792	-	3445261	65	YPK_3149				11	10		
YPK_TSS_793	+	3445646	38	YPK_3150	*folD*	13		13	11		
YPK_TSS_794	+	3446410	155	YPK_3151		26	19	23			
YPK_TSS_795	+	3448539	56	YPK_3153	*ppiB*	48		34			
YPK_TSS_796	+	3448998	102	YPK_3154		111	35	152	30	25	
YPK_TSS_797	+	3456700	25	YPK_3161	*ybbN*	14			13		
YPK_TSS_798	+	3457759	30	YPK_3162		12	16				
YPK_TSS_799	-	3459790	36	YPK_3164	*cueR*				23		
YPK_TSS_800	+	3459919	42	YPK_3165	*ATCU*		5				
YPK_TSS_801	+	3469402	45	YPK_3175	*rosB*	22	19	12	10		
YPK_TSS_802	-	3472572	33	YPK_3176	*gsk*	8	8	7			
YPK_TSS_803	-	3489226	332	YPK_3189	*ddhC*		11		10		
YPK_TSS_804	-	3492133	343	YPK_3192	*ddhD*		66		22		
YPK_TSS_805	-	3494152	68	YPK_3194	*adk*	72		25			
YPK_TSS_806	-	3496232	47	YPK_3195	*htpG*	38					
YPK_TSS_807	-	3497375	61	YPK_3197	*ybaB*	13					
YPK_TSS_808	-	3497640	326	YPK_3197	*ybaB*	31		52			
YPK_TSS_809	-	3499406	60	YPK_3198	*dnaX*		11				
YPK_TSS_810	-	3500755	190	YPK_3199	*apt*	19		11			
YPK_TSS_811	+	3501985	107	YPK_3203		20	27	25	22		
YPK_TSS_812	+	3507032	363	YPK_3207	*acrA*	35	74	17	19		
YPK_TSS_813	+	3507095	300	YPK_3207	*acrA*		15		12		
YPK_TSS_814	+	3507312	83	YPK_3207	*acrA*	26		31			
YPK_TSS_815	+	3514254	188	YPK_3213				33			
YPK_TSS_816	+	3514336	106	YPK_3213		33	21	13		105	
YPK_TSS_817	-	3517094	80	YPK_3216	*ybaY*	14	11	28	53	12	
YPK_TSS_818	+	3517246	25	YPK_3217	*tesB*	78	28	116	46	27	26
YPK_TSS_819	-	3524152	59	YPK_3222	*mdlA-2*		19		12	11	
YPK_TSS_820	+	3528343	609	YPK_3227	*ybaX*	17		32			
YPK_TSS_821	-	3530208	65	YPK_3228	*ybaW*		19		40		
YPK_TSS_822	-	3533183	214	YPK_3230	*ppiD*	12					
YPK_TSS_823	-	3533603	61	YPK_3231	*hupB*	150		390			
YPK_TSS_824	-	3533671	129	YPK_3231	*hupB*	183	83	240	27		
YPK_TSS_825	-	3536196	82	YPK_3232	*lon*	154	15	71	16		10
YPK_TSS_826	-	3536436	322	YPK_3232	*lon*	35	167	42	42	67	12
YPK_TSS_827	-	3538445	36	YPK_3234	*clpP*	119	49	175	39	25	
YPK_TSS_828	-	3538523	114	YPK_3234	*clpP*			11			
YPK_TSS_829	-	3538579	170	YPK_3234	*clpP*	14					
YPK_TSS_830	-	3540360	185	YPK_3235	*tig*	177		80			
YPK_TSS_831	-	3540532	99	YPK_3236		11					
YPK_TSS_832	-	3540951	39	YPK_3237	*bolA*		98		31	75	10
YPK_TSS_833	-	3540974	62	YPK_3237	*bolA*	23		28			
YPK_TSS_834	+	3541182	79	YPK_3238	*yajG*	37	19	42	24		
YPK_TSS_835	+	3543654	65	YPK_3240		39	47	45	27		
YPK_TSS_836	+	3544807	45	YPK_3241	*cyoA*	223	114	265	58		
YPK_TSS_837	+	3550103	22	YPK_3246	*yajR*	14					
YPK_TSS_838	-	3552130	26	YPK_3247	*yajQ*	22		22			
YPK_TSS_839	+	3552284	52	YPK_3248	*panE*		7	3	6	7	
YPK_TSS_840	-	3561653	34	YPK_3257	*ribH*	64					
YPK_TSS_841	-	3561661	42	YPK_3257	*ribH*	15		22			
YPK_TSS_842	-	3563474	29	YPK_3259	*ybaD*	86	40	135	24	24	
YPK_TSS_843	-	3568350	61	YPK_3263	*yajC*	51		17			
YPK_TSS_844	+	3571644	147	YPK_3267	*ahpC*	80	58	50	28		
YPK_TSS_845	+	3571658	133	YPK_3267	*ahpC*			58		60	24
YPK_TSS_846	-	3583772	145	YPK_3275	*phoR*	10	28	10	14	22	
YPK_TSS_847	-	3584382	41	YPK_3276	*phoB*	19		23			
YPK_TSS_848	-	3590804	147	YPK_3279	*yajF*	10					
YPK_TSS_849	-	3592447	30	YPK_3281	*yaiE*		21	14			
YPK_TSS_850	-	3596019	25	YPK_3285		93	49	40	91	42	
YPK_TSS_851	-	3600250	22	YPK_3289	*crl*	19	11	16			
YPK_TSS_852	-	3601589	54	YPK_3290	*frsA*	40	49	67		23	
YPK_TSS_853	-	3602180	60	YPK_3291	*gpt*	13		30			
YPK_TSS_854	+	3607805	94	YPK_3295	*pepD*	55	23	27		11	
YPK_TSS_855	-	3619456	214	YPK_3305	*nqrA*	86	101	115	72		
YPK_TSS_856	+	3619652	68	YPK_3306	*yafK*		16		23	11	
YPK_TSS_857	-	3622025	43	YPK_3308	*gmhA*	49		57		14	
YPK_TSS_858	+	3622178	43	YPK_3309	*fadE*			21	39		
YPK_TSS_859	+	3642148	30	YPK_3322	*ybdL*	11					
YPK_TSS_860	+	3656727	22	YPK_3337	*emrR*	32		16	35		
YPK_TSS_861	-	3661712	22	YPK_3340	*yfiF*	12					
YPK_TSS_862	+	3663298	32	YPK_3343	*yfiQ*		11	14	20		
YPK_TSS_863	+	3666080	68	YPK_3344	*pssA*	3		5			
YPK_TSS_864	-	3676681	31	YPK_3349	*clpB*	17	11		26		
YPK_TSS_865	+	3678233	393	YPK_3352	*yfiO*					11	
YPK_TSS_866	+	3678563	63	YPK_3352	*yfiO*	13	25	31		13	
YPK_TSS_867	+	3679678	34	YPK_3353	*yfiA*	241	57	650	68	45	38
YPK_TSS_868	-	3684416	508	YPK_3357	*aroF*	20	57	12			

tss id	strand	TSS position (+ strand)	Distance to start codon [nt]	Gene ID	name	Reads YPIII 25°C exp	Reads YPIII 25°C stat	Reads YPIII 37°C exp	Reads YPIII 37°C stat	Reads YP89 25°C stat	Reads YP89 37°C stat
YPK_TSS_869	+	3686914	36	YPK_3360	*ydiY*	18					
YPK_TSS_870	-	3690075	70	YPK_3364	*rpsP*	1163	40	360			
YPK_TSS_871	-	3690186	181	YPK_3364	*rpsP*	51	23			19	
YPK_TSS_872	-	3691639	45	YPK_3365	*ffh*	16	13	12			
YPK_TSS_873	+	3691728	32	YPK_3366	*ypjD*	22	16			13	
YPK_TSS_874	-	3691806	212	YPK_3365	*ffh*		10	11			
YPK_TSS_875	-	3694611	104	YPK_3368	*luxS*		25	12		12	
YPK_TSS_876	-	3698837	44	YPK_3372	*csrA*	107	51	112	23	110	18
YPK_TSS_877	-	3698920	127	YPK_3372	*csrA*		67		34	27	18
YPK_TSS_878	-	3701762	92	YPK_3373	*alaS*	162	29	12			
YPK_TSS_879	-	3703900	71	YPK_3375	*recA*	10					
YPK_TSS_880	+	3706312	25	YPK_3378		41		31			
YPK_TSS_881	+	3717277	26	YPK_3388	*katY*	20	87	795	99		
YPK_TSS_882	+	3727587	89	YPK_3397	*fucR*		20		39		
YPK_TSS_883	+	3736088	202	YPK_3404	*fumA*	20	35	45	12	11	
YPK_TSS_884	-	3754663	111	YPK_3421	*ydjJ*				25		
YPK_TSS_885	+	3754878	157	YPK_3422	*rpiB-1*				52		
YPK_TSS_886	+	3755005	30	YPK_3422	*rpiB-1*				32		
YPK_TSS_887	-	3760780	543	YPK_3425	*rpoS*	30	488	114	139	194	119
YPK_TSS_888	-	3765439	268	YPK_3431	*ispD*	13	93	29	95	28	46
YPK_TSS_889	-	3765513	18	YPK_3432	*ftsB*	18		10			
YPK_TSS_890	-	3765594	99	YPK_3432	*ftsB*	12			13		
YPK_TSS_891	-	3766321	194	YPK_3433	*ygbE*	18	19	25		31	
YPK_TSS_892	-	3770855	28	YPK_3437	*cysG*			44		70	
YPK_TSS_893	+	3771416	24	YPK_3438		35	152	40	12	16	20
YPK_TSS_894	-	3773837	637	YPK_3440	*cysH*		16	31	16		
YPK_TSS_895	-	3776810	81	YPK_3442	*cysJ*			8		7	
YPK_TSS_896	+	3777095	27	YPK_3443	*ygcM*	47		19			
YPK_TSS_897	-	3778414	28	YPK_3444	*ygcF*	12					
YPK_TSS_898	-	3779158	63	YPK_3445	*sodC*	117	35	458	30		
YPK_TSS_899	-	3781252	490	YPK_3446	*eno*	4	249		32	116	10
YPK_TSS_900	-	3782526	46	YPK_3447	*pyrG*	137		80			
YPK_TSS_901	+	3792830	47	YPK_3454	*mtn*	19		24			
YPK_TSS_902	-	3795704	24	YPK_3457	*yadR*	16		3			
YPK_TSS_903	-	3795759	79	YPK_3457	*yadR*	40	29	39	45	17	
YPK_TSS_904	-	3797276	24	YPK_3458	*yadQ*			11	29		
YPK_TSS_905	-	3797299	47	YPK_3458	*yadQ*		15				
YPK_TSS_906	+	3810220	57	YPK_3468	*dksA*	175		159			
YPK_TSS_907	+	3812014	82	YPK_3470	*pcnB*	22		11			
YPK_TSS_908	+	3816337	140	YPK_3474	*panD*	24	42	20	23		
YPK_TSS_909	-	3820403	189	YPK_3477	*yadG*	10					
YPK_TSS_910	-	3822053	71	YPK_3479	*hpt*	26	16	12		24	
YPK_TSS_911	-	3822107	125	YPK_3479	*hpt*	31	17	27			
YPK_TSS_912	+	3824087	24	YPK_3481	*yacC*	52	18	16	13	51	10
YPK_TSS_913	+	3824531	44	YPK_3482	*speE*	25		13			
YPK_TSS_914	-	3828155	23	YPK_3486			11	4	5		
YPK_TSS_915	-	3828217	85	YPK_3486		22	38	24	21	13	
YPK_TSS_916	-	3831275	228	YPK_3487	*acnB*	127	119	309	101	35	
YPK_TSS_917	-	3831432	385	YPK_3487	*acnB*		12	13	12	5	
YPK_TSS_918	-	3833848	106	YPK_3489	*lpdA*	119	36	351			
YPK_TSS_919	-	3839349	78	YPK_3492	*pdhR*	101	13	18			
YPK_TSS_920	+	3843709	31	YPK_3497	*nadC*	28	15	17			
YPK_TSS_921	-	3849631	70	YPK_3501	*guaC*	14	31	41			
YPK_TSS_922	+	3849649	-2	YPK_3502				15			
YPK_TSS_923	+	3849829	28	YPK_3503	*coaE*	30	13	37	21		
YPK_TSS_924	-	3859561	70	YPK_3513	*ftsZ*	30		60			
YPK_TSS_925	-	3865320	48	YPK_3518	*murG*	12					
YPK_TSS_926	-	3875333	54	YPK_3527	*mraZ*	32	12	21			
YPK_TSS_927	+	3876257	124	YPK_3528	*ygaW*		15				
YPK_TSS_928	-	3878087	125	YPK_3529	*fruR*		10				
YPK_TSS_929	-	3878276	314	YPK_3529	*fruR*	40	28	39	25		
YPK_TSS_930	-	3905716	29	YPK_3549						177	
YPK_TSS_931	-	3929512	215	YPK_3566						6	
YPK_TSS_932	+	3929615	39	YPK_3567						98	
YPK_TSS_933	+	3938657	436	YPK_3574	*apaG*		17		25	13	10
YPK_TSS_934	-	3949255	32	YPK_3583	*carA*	10		11			
YPK_TSS_935	-	3949327	104	YPK_3583	*carA*	42		51			
YPK_TSS_936	-	3956135	177	YPK_3588	*ileS*	14		19			
YPK_TSS_937	-	3956951	23	YPK_3589	*ribF*		17			11	
YPK_TSS_938	+	3957082	261	YPK_3590	*rpsT*	164	22	13			
YPK_TSS_939	+	3957212	131	YPK_3590	*rpsT*	320	17	77	11	11	
YPK_TSS_940	+	3957265	78	YPK_3590	*rpsT*	149		118			
YPK_TSS_941	-	3963393	39	YPK_3594	*dnaK*	68			21		
YPK_TSS_942	-	3963515	161	YPK_3594	*dnaK*	63			30		16
YPK_TSS_943	+	3963628	100	YPK_3595	*yaaH*	40					
YPK_TSS_944	-	3969289	31	YPK_3598	*mogA*	51	24	145	42		
YPK_TSS_945	-	3970528	29	YPK_3599	*talB*	82	28	157	22	107	16
YPK_TSS_946	-	3970606	107	YPK_3599	*talB*	52	18	27		16	
YPK_TSS_947	-	3977526	218	YPK_3604	*thrA*	164	78	64	14	30	10
YPK_TSS_948	+	3978115	296	YPK_3606	*arcA*	12	12		25		
YPK_TSS_949	+	3978201	210	YPK_3606	*arcA*	21		13			
YPK_TSS_950	-	3982575	30	YPK_3612	*trpR*	11					
YPK_TSS_951	-	3984848	147	YPK_3613	*slt*			10			
YPK_TSS_952	+	3988308	64	YPK_3615		25	57		16		
YPK_TSS_953	+	3990963	34	YPK_3618	*yjjK*	32	11	13			
YPK_TSS_954	-	3995390	22	YPK_3620	*nadR*	10					
YPK_TSS_955	-	4003883	346	YPK_3627	*deoC*	47		15			
YPK_TSS_956	-	4003956	419	YPK_3627	*deoC*					17	
YPK_TSS_957	-	4004027	490	YPK_3627	*deoC*		12				
YPK_TSS_958	-	4009238	156	YPK_3632	*osmY*		28			17	
YPK_TSS_959	-	4011086	87	YPK_3633	*prfC*	22					
YPK_TSS_960	-	4012033	31	YPK_3635	*holD*	10					

tss id	strand	TSS position (+ strand)	Distance to start codon [nt]	Gene ID	name	Reads YPIII 25°C exp	Reads YPIII 25°C stat	Reads YPIII 37°C exp	Reads YPIII 37°C stat	Reads YP89 25°C stat	Reads YP89 37°C stat
YPK_TSS_961	+	4014492	140	YPK_3638	*hmsT*		12				
YPK_TSS_962	-	4017524	112	YPK_3639					11		
YPK_TSS_963	-	4026659	15	YPK_3647		13		32			
YPK_TSS_964	-	4029864	146	YPK_3649	*ydeW*		15			11	
YPK_TSS_965	-	4029896	178	YPK_3649	*ydeW*			15			
YPK_TSS_966	+	4036334	45	YPK_3656				18			
YPK_TSS_967	-	4043331	57	YPK_3662		38	69	63	33		
YPK_TSS_968	+	4063637	223	YPK_3679	*pepA*	25	33	10	29	13	
YPK_TSS_969	+	4063689	171	YPK_3679	*pepA*	17	17	11	13		
YPK_TSS_970	+	4068993	31	YPK_3682	*yjgM*		10	21	13	22	
YPK_TSS_971	-	4070498	32	YPK_3683		15	10	25	12	31	
YPK_TSS_972	+	4072937	107	YPK_3686	*ddpA-2*		21		60		
YPK_TSS_973	+	4074601	107	YPK_3687			71				
YPK_TSS_974	+	4074665	43	YPK_3687		31	62	21	10	94	
YPK_TSS_975	-	4102334	-18	YPK_3714				19	13		
YPK_TSS_976	+	4110561	257	YPK_3720				15			
YPK_TSS_977	-	4115907	846	YPK_3724	*deaD*	48	137	30	30	13	4
YPK_TSS_978	-	4118464	90	YPK_3726	*pnp*	247	95	128	78	45	48
YPK_TSS_979	-	4118978	71	YPK_3727	*rpsO*	710	182	308	157	33	14
YPK_TSS_980	-	4126094	84	YPK_3733	*secG*	68		59			
YPK_TSS_981	-	4128488	72	YPK_3735	*folP*		20				
YPK_TSS_982	-	4130514	35	YPK_3736	*hflB*	46	20	61			
YPK_TSS_983	+	4131272	31	YPK_3738	*yhbY*	98	12	27		12	
YPK_TSS_984	-	4132358	158	YPK_3739	*greA*	14					
YPK_TSS_985	+	4137398	26	YPK_3744				14			
YPK_TSS_986	-	4139196	25	YPK_3746	*xtmA2*	19	33	25	34	81	
YPK_TSS_987	-	4143050	89	YPK_3753				22			
YPK_TSS_988	-	4146176	68	YPK_3757	*rplU*	21		47			
YPK_TSS_989	+	4146295	73	YPK_3758	*ispB*	13					
YPK_TSS_990	+	4146327	41	YPK_3758	*ispB*			24		10	
YPK_TSS_991	-	4149662	48	YPK_3761	*mdh*		11				
YPK_TSS_992	-	4149836	222	YPK_3761	*mdh*	28					
YPK_TSS_993	+	4150047	31	YPK_3762	*argR*	15			14		
YPK_TSS_994	+	4150881	56	YPK_3763	*yhcN*					31	20
YPK_TSS_995	+	4154232	33	YPK_3767	*ppa*	62	20	112			
YPK_TSS_996	-	4163802	83	YPK_3773			24	65	811	82	28
YPK_TSS_997	-	4163857	138	YPK_3773			10	13			
YPK_TSS_998	-	4165564	203	YPK_3775	*cysQ*	17	41	13	33		
YPK_TSS_999	-	4166066	705	YPK_3775	*cysQ*					5	
YPK_TSS_1000	-	4169309	31	YPK_3778	*fklB*	52	10	47			
YPK_TSS_1001	+	4169399	197	YPK_3779	*ytfB*	3					
YPK_TSS_1002	+	4169475	121	YPK_3779	*ytfB*					10	
YPK_TSS_1003	-	4172534	95	YPK_3784	*rpsF*	894		175			
YPK_TSS_1004	-	4172797	66	YPK_3785				17			
YPK_TSS_1005	-	4175808	35	YPK_3788	*aidB*	11	66	34	12		
YPK_TSS_1006	-	4181950	23	YPK_3793	*purA*	47	85	53	14	52	44
YPK_TSS_1007	-	4186696	90	YPK_3799	*hfq*	76	49	21		11	
YPK_TSS_1008	-	4187061	455	YPK_3799	*hfq*	19	26	28	19	27	14
YPK_TSS_1009	-	4187115	509	YPK_3799	*hfq*	107	174	90	170	37	12
YPK_TSS_1010	-	4196585	54	YPK_3808				14			
YPK_TSS_1011	+	4196602	129	YPK_3809		12					
YPK_TSS_1012	+	4208796	63	YPK_3819		24	51		24	20	
YPK_TSS_1013	-	4208837	38	YPK_3818	*efp*	20		19			
YPK_TSS_1014	-	4209165	366	YPK_3818	*efp*	7		32			
YPK_TSS_1015	-	4211028	295	YPK_3821		6	5	3			
YPK_TSS_1016	-	4213417	73	YPK_3823	*groES*	270		454			
YPK_TSS_1017	-	4213719	375	YPK_3823	*groES*	10		47	10		
YPK_TSS_1018	-	4214318	132	YPK_3824	*fxsA*	25			10		
YPK_TSS_1019	+	4214336	274	YPK_3825	*aspA*				10		
YPK_TSS_1020	+	4214489	121	YPK_3825	*aspA*	25	10	56			
YPK_TSS_1021	-	4214548	362	YPK_3824	*fxsA*	13	15		18		
YPK_TSS_1022	+	4217573	79	YPK_3827		15	35	17	18		
YPK_TSS_1023	+	4224907	114	YPK_3832			20				
YPK_TSS_1024	+	4229200	32	YPK_3837				11			
YPK_TSS_1025	-	4232603	35	YPK_3841	*rhaR*		30	34	14		
YPK_TSS_1026	-	4245467	171	YPK_3853	*tyrB*	13	37				
YPK_TSS_1027	+	4248255	142	YPK_3856	*qor*					11	
YPK_TSS_1028	-	4251576	80	YPK_3858		11	15	37			14
YPK_TSS_1029	+	4251724	24	YPK_3859		26	23	28		13	
YPK_TSS_1030	+	4253644	29	YPK_3862	*pslB*	75	18	74			
YPK_TSS_1031	-	4257247	41	YPK_3863	*ubiA*					23	
YPK_TSS_1032	-	4278307	50	YPK_3877	*terZ*	38	12	25	24		
YPK_TSS_1033	+	4321238	18	YPK_3921	*rcs*			18			
YPK_TSS_1034	-	4338122	29	YPK_3932	*pepQ*	13					
YPK_TSS_1035	+	4338375	45	YPK_3933	*fadB*		16	60	91		
YPK_TSS_1036	-	4344213	-7	YPK_3936		54	12				
YPK_TSS_1037	+	4344341	103	YPK_3937	*rfaH*	14	7	6			
YPK_TSS_1038	+	4344421	23	YPK_3937	*rfaH*				12	17	10
YPK_TSS_1039	-	4348665	37	YPK_3942	*tatA*	23		17			
YPK_TSS_1040	-	4350462	23	YPK_3943	*ubiB*		50				
YPK_TSS_1041	-	4351889	31	YPK_3945	*ubiE*	77	27	87	32		12
YPK_TSS_1042	-	4358414	47	YPK_3950	*udp*	59		39			
YPK_TSS_1043	-	4365959	26	YPK_3956			21		10		
YPK_TSS_1044	-	4367149	123	YPK_3957		48	14	47		11	
YPK_TSS_1045	-	4386800	43	YPK_3976	*rpoH*	351	96	352	205	181	54
YPK_TSS_1046	-	4386836	79	YPK_3976	*rpoH*	35		24			
YPK_TSS_1047	-	4387044	287	YPK_3976	*rpoH*	34	32	22		21	
YPK_TSS_1048	-	4392642	42	YPK_3983		14	14	17			
YPK_TSS_1049	+	4392806	84	YPK_3984	*yhhN*	24	55	22	27		
YPK_TSS_1050	-	4392808	208	YPK_3983		20		13			
YPK_TSS_1051	+	4396661	220	YPK_3987	*yhhQ*						16
YPK_TSS_1052	+	4396814	67	YPK_3987	*yhhQ*	85					

tss id	strand	TSS position (+ strand)	Distance to start codon [nt]	Gene ID	name	Reads YPIII 25°C exp	Reads YPIII 25°C stat	Reads YPIII 37°C exp	Reads YPIII 37°C stat	Reads YP89 25°C stat	Reads YP89 37°C stat
YPK_TSS_1053	+	4397586	93	YPK_3988	*drcB*		10			10	
YPK_TSS_1054	-	4412119	44	YPK_3999	*pldA*	24					
YPK_TSS_1055	-	4414927	135	YPK_4002	*corA*	35					
YPK_TSS_1056	-	4415039	247	YPK_4002	*corA*	94	10	20	3		
YPK_TSS_1057	-	4417641	112	YPK_4005					60		
YPK_TSS_1058	-	4417747	218	YPK_4005				38	53		
YPK_TSS_1059	+	4417860	97	YPK_4006		16	18	12	14		
YPK_TSS_1060	-	4424705	86	YPK_4012		7	5	3			
YPK_TSS_1061	+	4424725	28	YPK_4013	*cyaY*	14		20			
YPK_TSS_1062	-	4428002	133	YPK_4015	*cyaA*	16			19	35	
YPK_TSS_1063	-	4436753	186	YPK_4022	*wecG*	12		16			
YPK_TSS_1064	-	4451444	328	YPK_4034	*rho*	79	66	28	81	138	
YPK_TSS_1065	-	4451980	58	YPK_4035	*trxA*	61		50			
YPK_TSS_1066	-	4452020	98	YPK_4035	*trxA*	15	11			41	30
YPK_TSS_1067	-	4452298	376	YPK_4035	*trxA*		27				
YPK_TSS_1068	-	4457046	30	YPK_4038	*rep*	21		26			
YPK_TSS_1069	+	4457146	59	YPK_4040	*ppiC*	58		14			
YPK_TSS_1070	-	4481056	274	YPK_4061	*ilvG*	10	13				
YPK_TSS_1071	+	4483454	188	YPK_4064	*hdfR*	15	14				
YPK_TSS_1072	-	4483562	39	YPK_4063		83		114		10	
YPK_TSS_1073	-	4498938	315	YPK_4073	*btuB*	16				11	
YPK_TSS_1074	+	4499048	37	YPK_4074	*trmA*	12					
YPK_TSS_1075	-	4501420	43	YPK_4076	*trmA*	11					
YPK_TSS_1076	+	4501564	31	YPK_4078	*sthA*	20	53	61	16	20	14
YPK_TSS_1077	+	4528292	240	YPK_4096	*metJ*	3	4		3		
YPK_TSS_1078	+	4528489	43	YPK_4096	*metJ*	51	20	52			
YPK_TSS_1079	-	4530501	108	YPK_4098	*rpmE*					28	
YPK_TSS_1080	-	4530525	132	YPK_4098	*rpmE*	276		190			
YPK_TSS_1081	-	4530565	172	YPK_4098	*rpmE*	15					
YPK_TSS_1082	+	4535168	68	YPK_4103	*hslV*	22			14		
YPK_TSS_1083	+	4538430	26	YPK_4106	*menG*	17	14	23	14		14
YPK_TSS_1084	-	4539861	219	YPK_4107						18	
YPK_TSS_1085	-	4540571	60	YPK_4108		22	60	28	12	282	
YPK_TSS_1086	-	4544806	103	YPK_4111	*zapB*	113	16	164		14	
YPK_TSS_1087	+	4545359	68	YPK_4112	*glpF*	846	13	63	21		
YPK_TSS_1088	-	4550964	99	YPK_4116		10		10			
YPK_TSS_1089	+	4551053	26	YPK_4117		9	4	3	8		
YPK_TSS_1090	+	4551778	65	YPK_4118	*tpiA*	58					
YPK_TSS_1091	-	4564319	38	YPK_4131	*cpxP*	15	11	17	40		
YPK_TSS_1092	+	4564439	16	YPK_4132	*cpxR*	11					
YPK_TSS_1093	+	4567810	18	YPK_4135	*trmL, cspR*	11					
YPK_TSS_1094	-	4571950	40	YPK_4140		11					
YPK_TSS_1095	+	4573864	0	YPK_4142		41	28	29	20	21	
YPK_TSS_1096	-	4578680	28	YPK_4145	*kbl*	33	38	192	28		
YPK_TSS_1097	+	4578843	55	YPK_4146	*rfaD*	37		30	10		
YPK_TSS_1098	+	4582285	-17	YPK_4149	*kdtA*		31			18	
YPK_TSS_1099	-	4586234	75	YPK_4154	*rpmB*	1254	45	607		115	
YPK_TSS_1100	-	4586343	184	YPK_4154	*rpmB*	154	13	12			
YPK_TSS_1101	-	4586569	410	YPK_4154	*rpmB*	24		11		12	
YPK_TSS_1102	-	4586649	490	YPK_4154	*rpmB*	164	62	74	18	12	
YPK_TSS_1103	-	4587118	28	YPK_4155	*radC*		10	17	14		
YPK_TSS_1104	+	4587259	28	YPK_4156	*dfp*			13			
YPK_TSS_1105	-	4591350	30	YPK_4160	*rph*	18		11			
YPK_TSS_1106	+	4591419	28	YPK_4161		31		33		10	
YPK_TSS_1107	+	4592421	77	YPK_4162		19	16	28	40		
YPK_TSS_1108	+	4604393	323	YPK_4176	*gmk*	26	11	13	12	28	14
YPK_TSS_1109	+	4604546	170	YPK_4176	*gmk*	75	18		13	21	
YPK_TSS_1110	+	4605364	30	YPK_4177	*rpoZ*	45	16				
YPK_TSS_1111	+	4613896	30	YPK_4183			14	10		10	
YPK_TSS_1112	-	4618917	23	YPK_4187	*yrfG, yigB*		12			17	
YPK_TSS_1113	-	4621070	31	YPK_4188	*bipA*	191		68		12	
YPK_TSS_1114	-	4621223	184	YPK_4188	*bipA*	17					
YPK_TSS_1115	-	4621277	238	YPK_4188	*bipA*	70		30			
YPK_TSS_1116	+	4621481	120	YPK_4189	*glnA*	10					
YPK_TSS_1117	+	4621515	86	YPK_4189	*glnA*	69		17			
YPK_TSS_1118	-	4627941	33	YPK_4193		31		31			
YPK_TSS_1119	-	4628034	126	YPK_4193		22		23			
YPK_TSS_1120	+	4628620	32	YPK_4194		13					
YPK_TSS_1121	-	4632540	32	YPK_4195	*polA*	19	15	30	10		
YPK_TSS_1122	-	4635022	26	YPK_4198		27	13	45			
YPK_TSS_1123	-	4647572	30	YPK_4210		23	68	79	15		
YPK_TSS_1124	+	4649739	150	YPK_4212						16	
YPK_TSS_1125	-	4654032	44	YPK_4214	*asnA*	16		12	11		
YPK_TSS_1126	+	4654687	25	YPK_4216	*mioC*	14	34	41		28	
YPK_TSS_1127	+	4655488	45	YPK_4217	*gidA*	15		11			
YPK_TSS_1128	+	4658768	86	YPK_4219	*atpI*	45		18			
YPK_TSS_1129	+	4666544	26	YPK_4228	*glmU*	25		13			
YPK_TSS_1130	+	4668028	113	YPK_4229	*glmS*	73	12	25		20	
YPK_TSS_1131	+	4668089	52	YPK_4229	*glmS*			26			
YPK_TSS_1132	+	4670272	181	YPK_4231	*pstS*	43		28			
YPK_TSS_1133	+	4670288	165	YPK_4231	*pstS*		15				
YPK_TSS_1134	+	4676382	33	YPK_4237				16		15	12
YPK_TSS_1135	-	4679671	34	YPK_4240						11	
YPK_TSS_1136	+	4680099	31	YPK_4241	*yieG*	32		16			
YPK_TSS_1137	-	4686284	83	YPK_4245	*trmE*	10					
YPK_TSS_1138	-	4688828	102	YPK_4249	*rpmH*	253	17	110	34	64	
YPK_TSS_1139	-	4688991	265	YPK_4249	*rpmH*	79	23	15			

Table S 12: Crp binding sites predicted for sRNAs.

ID	Strand	Crp_start	Crp_stop	Motif up	Motif spacer	Motif down	Mismatch up	Mismatch down	Mismatch sum	sRNA	Product
YPK_CRP_BS_12	-	329019	329034	TGTGA	CTAAGC	TAACA	0	1	1	YPK_asRNA_3	unknown
YPK_CRP_BS_31	+	688732	688747	TGTGA	AACCGG	GCAAA	0	2	2	YPK_transRNA_10	unknown
YPK_CRP_BS_39	+	1154325	1154340	TGCGA	TGCTAC	TCACG	1	1	2	YPK_transRNA_16	OmrA/B
YPK_CRP_BS_41	+	1196310	1196325	TGTGC	GAGATC	TCTCA	1	1	2	YPK_transRNA_19	CsrB
YPK_CRP_BS_42	+	1196312	1196327	TGCGA	GATCTC	TCACA	1	0	1	YPK_transRNA_19	CsrB
YPK_CRP_BS_48	-	1454729	1454744	TTAGA	AATAGA	TCACA	2	0	2	YPK_transRNA_25	CyaR (RyeE)
YPK_CRP_BS_63	+	1785790	1785805	CGTGA	TGTTTG	TCACA	1	0	1	YPK_asRNA_14	unknown
YPK_CRP_BS_72	-	2081821	2081836	TGTAA	ATTAAT	TCAAA	1	1	2	YPK_transRNA_33	unknown
YPK_CRP_BS_82	+	2237488	2237503	TGTGA	TCGATC	TCTCG	0	2	2	YPK_asRNA_21	unknown
YPK_CRP_BS_86	-	2310358	2310373	TGTGA	TGTGCG	TCACA	0	0	0	YPK_transRNA_38	unknown
YPK_CRP_BS_87	-	2310416	2310431	TGTGA	TGGATA	TCACA	0	0	0	YPK_transRNA_38	unknown
YPK_CRP_BS_91	-	2362969	2362984	TTTTA	GGCGTA	TCACA	2	0	2	YPK_transRNA_40	unknown
YPK_CRP_BS_97	+	2610057	2610072	TGTAA	TGCCGA	TAACA	1	1	2	YPK_asRNA_25	unknown
YPK_CRP_BS_100	+	2670769	2670784	TGTGA	GGGAGT	ACACA	0	1	1	YPK_transRNA_45	unknown
YPK_CRP_BS_105	-	2811499	2811514	TGCGA	GTTAAC	TTACA	1	1	2	YPK_transRNA_49	unknown
YPK_CRP_BS_113	-	2966582	2966597	TGTGA	TGGTCG	CCGCA	0	2	2	YPK_asRNA_30	unknown
YPK_CRP_BS_121	+	3119472	3119487	TCTGT	AACACA	TCACA	2	0	2	YPK_transRNA_54	unknown
YPK_CRP_BS_122	+	3119498	3119513	GGTGA	TCCTTC	TCACA	1	0	1	YPK_transRNA_54	unknown
YPK_CRP_BS_123	+	3119570	3119585	TGCCA	CTATTG	TCACA	2	0	2	YPK_transRNA_54	unknown
YPK_CRP_BS_129	+	3262295	3262310	AGTGA	GTCAAA	TCACA	1	0	1	YPK_transRNA_56	unknown
YPK_CRP_BS_139	-	3464013	3464028	TATGC	TGGTGC	TCACA	2	0	2	YPK_transRNA_60	MicM (SroB)
YPK_CRP_BS_142	-	3515660	3515675	TGTGA	ACTCGG	TCAGG	0	2	2	YPK_transRNA_61	SRP
YPK_CRP_BS_151	+	3694639	3694654	TGTTA	ATTTGG	CCACA	1	1	2	YPK_transRNA_65	MicA (SraD)
YPK_CRP_BS_160	-	3988268	3988283	TGTAA	TAATAG	TCATA	1	1	2	YPK_asRNA_49	unknown
YPK_CRP_BS_161	+	4005510	4005525	AGTAA	TCTCCG	TCACA	2	0	2	YPK_transRNA_71	unknown
YPK_CRP_BS_162	+	4005556	4005571	TGTAA	ATGTGA	TCATA	1	1	2	YPK_transRNA_71	unknown
YPK_CRP_BS_163	+	4005562	4005577	TGTGA	TCATAA	TCACA	0	0	0	YPK_transRNA_71	unknown
YPK_CRP_BS_164	+	4005601	4005616	TGTGA	GGTTAT	TGACA	0	1	1	YPK_transRNA_71	unknown
YPK_CRP_BS_168	-	4072904	4072919	TGTGG	TAAAAG	TCTCA	1	1	2	YPK_transRNA_73	unknown
YPK_CRP_BS_180	+	4210910	4210925	AGTGA	TTCGGG	TGACA	1	1	2	YPK_asRNA_56	unknown
YPK_CRP_BS_182	-	4249657	4249672	TGCGG	CAGCGA	TCACA	2	0	2	YPK_transRNA_74	unknown